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WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM

Date: September 27, 2018

SUBJECT: MCPA. Draft Human Health Risk Assessment in Support of Registration Review.

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1.0 Executive Summary

Background

MCPA (4-chloro-o-tolyloxyacetic acid) is a selective, post-emergence systemic herbicide used for the control of annual and perennial broadleaf weeds. MCPA belongs to the phenoxy or phenoxyacetic acid family. Phenoxy herbicides act by simulating the action of natural plant hormones and produce uncoordinated cell division and plant growth. MCPA is registered for use on residential lawns, ornamental turf and trees, golf courses, parks, roadsides, rights of way; and for agricultural use on alfalfa, barley, clover, flax, oats, pasture and rangeland grass, peas, rye, triticale, wheat, and grass grown for seed.

Exposure to MCPA may occur from ingestion of residues in foods and in drinking water. There is the potential for dermal and inhalation exposure for adults (handlers) who mix and or apply MCPA. Exposure may also occur for adults (dermal) and children (dermal, incidental oral, episodic oral) who enter residential areas that have been previously treated with MCPA, such as lawns and golf courses. In addition, there is the potential for exposure to spray drift from agricultural applications onto non-occupational sites such as lawns. The Health Effects Division (HED) has conducted a human health risk assessment to support the Registration Review of MCPA. Assessments were performed for potential dietary, residential, aggregate, non-occupational spray drift, and occupational exposures.

Based on the currently registered uses of MCPA, the durations of exposure are expected to be both short- (1 to 30 days) and intermediate-term (1 to 6 months) for occupational handlers. Residential handler, post-application, and spray drift exposure durations are expected to be short-term only. Most, but not all, labels require baseline clothing (i.e., single layer clothing: long-sleeved shirt, long pants, shoes plus socks) and varying levels of additional personal protective equipment (PPE), such as respirators, chemical-resistant gloves, chemical-resistant aprons, coveralls (double layer), and chemical-resistant footwear. Additionally, the emulsifiable concentrate end-use products require the use of a closed-system (engineering controls- EC) when mixing and loading the product for aerial application.

For tolerance enforcement, the residue of concern is MCPA. For risk assessment purposes, the residue of concern in livestock commodities is MCPA, but in plant commodities the residues of concern include both MCPA and its metabolite 2-HMCPA [(4-chloro-2-hydroxymethylphenoxy)acetic acid]. The residue of concern in drinking water is MCPA. MCPA is a metabolite of MCPB (4-(4-chloro-2-methylphenoxy)butanoic acid), which is also a pesticide active ingredient. A separate human health risk assessment will be issued for MCPB.

Formulations of MCPA are available in acid, salt, amine, or ester forms. The active ingredients are MCPA acid (MCPA; PC code 030501), MCPA sodium salt (MCPA Na; PC code 030502), MCPA dimethylamine salt (MCPA DMA; PC code 030516), and MCPA 2-ethylhexyl ester (MCPA 2-EHE; PC code 030564). HED's Hazard Identification Assessment Review Committee (HIARC) concluded that the toxicity of all forms of MCPA were essentially identical. The

toxicity database for MCPA is complete for assessing all formulations of MCPA (acid, salt, amine, and ester) (TXR# 0052196, P. Chin, 10/29/2003; HIARC report).

Hazard

The kidney is the major target organ following MCPA exposure. In the subchronic inhalation toxicity study, respiratory tract effects were observed following repeat inhalation exposure. Additional toxic effects include neurotoxicity, which was observed in the acute and subchronic neurotoxicity (ACN/SCN) studies and in a rat developmental toxicity study. The developmental neurotoxicity study (DNT) did not identify developmental neurotoxicity.

Quantitative susceptibility was observed in the rat developmental toxicity study with MCPA acid based on increased incidence of skeletal retardation and decreased fetal body weight at a dose that was a maternal No Observed Adverse Effect Level (NOAEL). There was also quantitative susceptibility in the two-generation rat reproductive toxicity study with MCPA acid as evidenced by decreased lactational pup body weight at an offspring Lowest Observed Adverse Effect Level (LOAEL) corresponding to a parental NOAEL. Qualitative susceptibility was noted in the DNT study based on increased pup mortality and body weights at the same LOAEL as the maternal LOAEL (decreased body weight and food consumptions).

MCPA is classified as "*Not Likely to Be Carcinogenic to Humans,*" based on long-term studies in rats and mice, and there are low mutagenicity concerns. There is no concern for immunotoxicity, and it has been recommended that the immunotoxicity testing be waived (TXR# 0056819, J. Leshin, 11/5/2013).

The MCPA risk assessments are based on the most sensitive endpoints in the toxicity database, and the points of departure (PODs) selected for risk assessment are considered protective of any potential adverse effects, including developmental and neurotoxic effects for infants and children. For acute dietary (females 13-49 years old), chronic dietary, incidental oral, and residential dermal exposures, the Food Quality Protection Act (FQPA) safety factor (SF) is reduced to 1X. However, for acute dietary (general population including infants and children), acute oral (episodic ingestion), and residential inhalation exposures a 10X FQPA SF is retained as an uncertainty factor (UF) for the use of a LOAEL to extrapolate to a NOAEL (UF_L).

The residential/occupational dermal and residential incidental oral level of concern (LOC) is 100, which includes a 10X interspecies extrapolation UF and a 10X intraspecies variability UF. The dermal absorption factor (DAF) is 22%. The residential/occupational inhalation LOC is 300, which includes the following UFs: 3X interspecies extrapolation, 10X intraspecies variability, and a 10X FQPA(residential)/UF_L (occupational); the standard interspecies extrapolation UF is reduced from 10X to 3X because a route-specific study is available and the calculation of human equivalent concentrations accounts for pharmacokinetic differences between human and the experimental species used in the selected study (rat). The residential acute oral (episodic ingestion) LOC is 1000, which includes the following UFs: 10X interspecies extrapolation, 10X intraspecies variability, and a FQPA SF as a UF_L (10X).

For MCPA, it is possible to combine incidental oral and dermal exposures because those routes

have a common toxicological endpoint (decreased pup weight during lactation). However, the inhalation exposure endpoint is respiratory tract effects, so the inhalation exposure cannot be combined with either oral or dermal exposures.

Dietary

Unrefined acute and chronic dietary (food and drinking water) risk assessments were conducted using tolerance-level residues in food and 100% crop treated (CT) for all commodities. Default food processing factors were used. For drinking water, high-end estimated drinking water concentrations (EDWCs) were derived from modeling based on the highest labeled use rates and most vulnerable areas. All acute and chronic dietary (food and drinking water combined) risk estimates do not exceed the level of concern (100% of the acute or chronic population adjusted dose (aPAD or cPAD)) for the general U.S. population and all population subgroups. The acute risk estimates at the 95th percentile of exposure are 10% of the aPAD for the U.S. population, and 29% of the aPAD for infants (the most highly exposed population subgroup). The chronic dietary risk estimates are 12% of the cPAD for the U.S. population, and 28% of the cPAD for infants (the most highly exposed population subgroup).

Residential

The residential handler dermal and inhalation margins of exposure (MOEs) are all greater than the LOC (dermal LOC is 100 and inhalation LOC is 300) and are not of concern. Dermal MOEs range from 260 to 10,000,000. Inhalation MOEs range from 5,200 to 2,600,000.

Chemical specific turf transferable residue (TTR) data for liquids are available for MCPA and were used to assess exposures from liquid formulations only (default assumptions were used for the granular formulations). Using Day 0 predicted TTR values for liquid formulations and Day 0 default TTR assumptions for granular formulations, all residential post-application scenarios are not of concern (MOEs are greater than the LOC of 100), except exposures from high contact lawn activities for adults (on lawns treated with liquid formulations) and children (1 to <2 years old) (on lawns treated with liquid or granular formulations). For adults, the dermal MOE resulting from high contact activity is 67 for liquid formulations. For children, the dermal MOE resulting from high contact activity is 34 for liquid formulations. The combined (dermal and incidental oral) MOEs for children resulting from high contact activity are 31 for liquid formulations and 85 for granules. The episodic granule ingestion scenario for children is of concern (MOE is less than the LOC of 1000) with an MOE of 860.

Use of Day 0 chemical-specific TTR values in the residential post-application assessment is considered a screening level, conservative approach. Since this approach has resulted in risk estimates of concern for high contact lawn activity scenarios for the liquid formulations, HED has considered the modeled daily residue dissipation from the available MCPA TTR liquid formulation data to further characterize residential post-application exposures. When considering a 6-day average, the short-term residential post-application risk estimates for high contact activities are not of concern for adults and children. The adult MOE is 220 and the child combined (dermal and incidental oral) MOE is 100. Since the 6-day average TTR refinement resulted in a combined (dermal and incidental oral) MOE of 100, which cannot be aggregated

with dietary exposure as there is no room available in the 'risk cup' for any additional exposures, HED has back-calculated the minimum number of days the TTR data would need to be averaged in order to reach an aggregate risk estimate that is not of concern. It was determined that an 8-day average TTR results in a combined (dermal and incidental oral) MOE of 120 for children (which results in an aggregate MOE of 110), and is not of concern. Averaging TTR values over this duration of exposure is scientifically defensible since the risk assessment endpoint and point of departure for these scenarios is taken from a reproduction study which represent dosing of animals over many weeks. Therefore, averaging residential exposure over this time frame (by using average TTR values) is appropriate. While HED has determined that aggregate risks are acceptable using an 8-day averaging time, further refinements are possible since animals in the reproduction study were dosed for longer durations than 8 days.

Aggregate

The acute and chronic aggregate risk assessments include food and drinking water only. There are no acute or chronic aggregate risk estimates of concern for the registered uses of MCPA.

The short-term aggregate risk assessments include residential exposures and average dietary (food and water) exposures. Residential exposure scenarios for children 1 to <2 years old (for both the liquid and granular formulations) that resulted in risk estimates of concern (when using Day 0 TTR values) are not included in this aggregate assessment as combining those exposures with dietary exposures would result in even greater risk estimates of concern. The selected residential exposure scenarios for aggregation, adults conducting high contact lawn activities (granules) and children playing golf (liquid formulation), represent the worst-case risk estimates of the residential scenarios that were determined not to be of concern. A short-term aggregate assessment (using 0-day TTR) has not been conducted for children 1 to <2 years old since residential scenarios for both the liquid and granular formulations result in risks of concern. For the scenarios assessed, the short-term aggregate MOEs for adults (190), children 6 to <11 years old (330), and children 11 to <16 years old (390) are above the LOC (100) and are not of concern.

For the residential exposure scenarios with liquid formulations that resulted in risk estimates of concern (when using Day 0 chemical-specific TTR values), an aggregate assessment was performed incorporating the residential exposures estimated using the refinement of a 6-day average TTR. Those scenarios are adult and children, high contact activities on lawns treated with liquid formulations. Using 6-day average TTR, the short-term aggregate MOE for adults is 190 and is not of concern. However, the child MOE of 88 is below the LOC of 100 and is of concern.

For the residential exposure scenario that resulted in a risk estimate of concern when using the refined 6-day TTR average value (children high contact activities on lawns treated with liquid) HED has back-calculated the minimum number of days over which the TTR data would need to be averaged in order to result in an aggregate risk estimate that is not of concern; it was determined that a minimum 8-day average TTR results in an aggregate MOE above the LOC of 100. With the 8-day average TTR, the MOE for children is 110 and is not of concern.

Spray Drift

There is the potential for non-occupational post-application exposure from spray drift. For children, dermal and incidental oral risk estimates from indirect exposure to MCPA related to spray drift were not of concern at the field edge. Adult dermal risk estimates from spray drift are not of concern at the field edge.

Occupational

Most occupational handler scenarios are not of concern (MOEs are greater than the LOC; dermal LOC is 100 and inhalation LOC is 300) with baseline personal protective equipment (PPE) and engineering controls (for aerial applications); however, several scenarios are still of concern with label-specified PPE (i.e., single layer clothing: long-sleeved shirt, long pants, shoes plus socks) and additional PPE such as respirators, chemical-resistant gloves, chemical-resistant aprons, coveralls (double layer), and chemical resistant footwear. Dermal exposures are driving risk estimates for most scenarios.

All occupational post-application scenarios are not of concern on the day of application (MOEs are greater than the dermal LOC of 100) except irrigation (handset) for forage crop (which is no longer of concern 11 days after treatment (DAT)), and scouting for forage crop (which is no longer of concern 5 DAT).

Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for MCPA at this time. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for MCPA.

Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment (see Section 3.5).

Human Data

See Appendix D for information regarding the use of human research data in this assessment.

2.0 HED Conclusions

There are no dietary (food and drinking water) or residential handler risk estimates of concern. There are residential post-application risk estimates of concern for exposures from high contact lawn activities for adults (liquid formulation) and children (liquid and granular formulations). HED has back-calculated the minimum number of days the chemical-specific TTR data for liquid formulations would need to be averaged in order to reach risk estimates that are not of concern for the liquid scenarios. It was determined that an 8-day average TTR results in a combined (dermal and incidental oral) MOE of 120 for children (which results in a short-term aggregate MOE of 110), and is not of concern. Refinement for the child exposure from high

contact lawn activities for the granular formulation was not possible as only default TTR data were available for granules. The episodic granule ingestion scenario for children is of concern (MOE is less than the LOC of 1000) with an MOE of 860. Indirect exposure to MCPA as a result of spray drift are not of concern for children and adults at the field edge. There are occupational handler scenarios that are of concern even when considering additional PPE; dermal exposures are driving the risk estimates for these scenarios. All occupational post-application scenarios are not of concern on the day of application except irrigation (handset) for forage crop (which is no longer of concern 11 DAT, and scouting for forage crop (which is no longer of concern 5 DAT).

2.1 Data Deficiencies

Residue Chemistry

There are adequate residue data to support the application of MCPA to small grains underseeded with alfalfa or clover (D427332, D. Drew, 5/27/2017). There are no residue data to support the direct application of MCPA to alfalfa and clover stands, which could result in higher residues than applications to an underseeded crop. Current tolerances listed for alfalfa and clover are based on data for the small grains underseeded uses and do not reflect potential residues resulting from direct application to alfalfa and clover. The uses for direct application to alfalfa and clover should be removed from the MCPA labels. Alternatively, appropriate alfalfa and clover crop field trials should be performed according to the 860.1500 Guideline in order to retain a direct application use.

Residential and Occupational

Chemical-specific dislodgeable foliar residue (DFR) data (Guideline 875.2100) are not available for MCPA (these data were originally requested in HED's memorandum *MCPA Human Health Risk Assessment Scoping Document in Support of Registration Review*, D414988, A. LaMay, 2/6/2014). Since the highest estimated occupational post-application exposure using default DFR values for MCPA is not minimal in comparison to the level of concern (i.e., the calculated MOE is not greater than 2 times higher than the level of concern, MOE = 100 (DAT5) compared to the LOC of 100) these 40 CFR 158 data should be submitted. The DFR data will facilitate any necessary exposure assessment refinements and will further EPA's general understanding of the availability of dislodgeable foliar pesticide residues.

Liquid TTR data are available for MCPA, and were used to represent liquid formulations in the post-application assessment. Default TTR data were used for granular formulations in the post-application assessments. Submitting TTR data on the granular formulation would help refine the assessment for that formulation.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

For enforcement of tolerances for residues of MCPA, PAM Vol. II lists PAM Vol. I Sections 221.1, 421, and 422. No limit of quantitation is specified. It is noted that Section 221.1 has now become Section 402 (gas chromatography (GC) method for acids and phenols) and Sections 421 and 422 (thin-layer chromatography (TLC) methods) no longer exist. The Residue Chemistry Chapter of the Registration Standard dated 8/31/1981 noted that the PAM Vol. I method is adequate for enforcement of tolerances for residues of MCPA in livestock commodities as-is, but recommended that the method be modified with a hydrolysis step for enforcement of MCPA tolerances for plant commodities. The current PAM Vol II methods are adequate for the enforcement of MCPA on plants and livestock commodities and no further modifications are required at this time. The data requirement for 860.1340 residue analytical methods is fulfilled.

The analytical standard for MCPA (CAS # 94-74-6) is available at the EPA National Pesticide Standards Repository with an expiration date of April 21, 2020 [email communication from G. Verdin, July 19, 2018]. A fresh reference standard can be provided to the Repository, and then replenished as requested by the Repository. The reference standard should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, to the attention of Theresa Cole at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

The full 9-digit zip code is mandatory or the mail will be returned.

2.2.2 Recommended Tolerances

Tolerances for residues of MCPA are currently expressed in 40 CFR §180.339 in terms of parent compound MCPA, which is the residue of concern for enforcement in both plant and livestock commodities. The tolerance definition for MCPA residues should be updated to comply with *Guidance on Tolerance Expressions* (S. Knizer, 5/27/2009) to read as follows:

> *"(a) General. Tolerances are established for residues of the herbicide MCPA, including its metabolites and degradates, in or on the commodities in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only MCPA, 2-(4-chloro-2-methylphenoxy)acetic acid, in or on the commodity.*"

Currently, plant commodities are listed in the table in 40 CFR 180.339(a)(1) and livestock commodities are listed in the table under 40 CFR 180.339(a)(2). HED recommends that both plant and livestock commodities be listed under 40 CFR 180.339(a)(1) as the tolerance expression is the same for plant and livestock commodities. A summary of the MCPA tolerance reassessment for the livestock and crop commodities and recommended modifications in commodity definitions are presented in Table 2.2.2.

Table 2.2.2. Tolerance Summary for MCPA under 40 CFR 180.339(a)(1).			
Commodity/Correct Commodity Definition	**Established Tolerance (ppm)**	**HED-Recommended Tolerance (ppm)**	**Comments**
Alfalfa, forage	0.5	0.50	Corrected value to be consistent with HED Rounding Class Practice.
Alfalfa, hay	2.0	2.0	
Barley, grain	1.0	0.20	Updated OECD calculation. Harmonization with Codex
Barley, hay	40	50	Harmonization with Codex
Barley, straw	25	50	Harmonization with Codex
Cattle, fat	0.1	0.20	Updated dietary burden calculation. Harmonization with Codex
Cattle, meat	0.1	0.10	
Cattle, meat byproducts	0.1	3.0	
Clover, forage	0.5	0.50	Corrected value to be consistent with HED Rounding Class Practice.
Clover, hay	2.0	2.0	
Flax, seed	0.1	0.01	Updated residue data. Harmonization with Codex
Goat, fat	0.1	0.20	Updated dietary burden calculation. Harmonization with Codex
Goat, meat	0.1	0.10	
Goat, meat byproducts	0.1	3.0	
Grain, aspirated fractions	3.0	3.0	
Grass, forage, fodder, and hay, Group 17, forage	-	500	Updated OECD calculation. Updated to Group Tolerance. Harmonization with Codex
Grass, forage	300	Remove	
Grass, forage, fodder, and hay, Group 17, hay	-	200	Updated OECD calculation. Updated to Group Tolerance
Grass, hay	20	Remove	
Hog, fat	0.1	Remove	Updated dietary burden calculation. No expectation of quantifiable residues
Hog, meat	0.1	Remove	
Hog, meat byproducts	0.1	Remove	
Horse, fat	0.1	0.20	Updated dietary burden calculation. Corrected value to be consistent with HED Rounding Class Practice. Harmonization with Codex
Horse, meat	0.1	0.10	
Horse, meat byproducts	0.1	3.0	
Lespedeza forage	0.5	0.50	Corrected value to be consistent with HED Rounding Class Practice.
Lespedeza, hay	2.0	2.0	

Table 2.2.2. Tolerance Summary for MCPA under 40 CFR 180.339(a)(1).			
Commodity/Correct Commodity Definition	**Established Tolerance (ppm)**	**HED-Recommended Tolerance (ppm)**	**Comments**
Milk	0.1	0.04	Updated dietary burden calculation. Harmonization with Codex
Oat, forage	20	50	Harmonization with Codex
Oat, grain	1.0	0.20	Updated OECD calculation. Harmonization with Codex
Oat, hay	115	50	Updated OECD calculation. Harmonization with Codex
Oat, straw	25	50	Harmonization with Codex
Pea, dry, seed	-	0.01	Commodity definition revision. Updated field trial data. Updated OECD calculation. Harmonization with Codex
Pea, dry	0.1	remove	
Pea, field, hay	0.1	1.5	Updated field trail data. Updated OECD calculation
Pea, succulent shelled	-	0.10	Commodity definition revision. Corrected value to be consistent with HED Rounding Class Practice.
Pea, succulent	0.1	remove	
Pea, field, vines	0.1	0.60	Updated field trail data
Rye, forage	20	50	Harmonization with Codex
Rye, grain	1.0	0.20	Updated OECD calculation. Harmonization with Codex
Rye, straw	25	50	Harmonization with Codex
Sheep, fat	0.1	0.20	Updated dietary burden calculation. Corrected value to be consistent with HED Rounding Class Practice. Harmonization with Codex
Sheep, meat	0.1	0.10	
Sheep, meat byproducts	0.1	3.0	
Trefoil, forage	0.5	0.50	Corrected value to be consistent with HED Rounding Class Practice.
Trefoil, hay	2.0	2.0	
Vetch, forage	0.5	0.50	Corrected value to be consistent with HED Rounding Class Practice.
Vetch, hay	2.0	2.0	
Wheat, forage	20	50	Harmonization with Codex
Wheat, grain	1.0	0.20	Updated OECD calculation. Harmonization with Codex
Wheat, hay	115	50	Updated OECD calculation. Harmonization with Codex
Wheat, straw	25	50	Harmonization with Codex

Basis for Recommended Tolerances:

The MCPA Task Force Three submitted a crop field trial study reflecting the use of MCPA on dry peas (MRID 50107601; Guideline 860.1500) in response to outstanding residue chemistry data requirements. HED has evaluated the dry pea data submitted, along with existing field trial data on succulent peas, and concluded that there was sufficient data with adequate geographical

representation to support a national use of MCPA on peas, and to support the current tolerance of 0.10 ppm for succulent peas. Dry pea residues from field trials were <0.010 ppm following applications approximating the 1x rate. These data indicate that the current tolerance of 0.1 ppm for pea, dry is too high, and a tolerance at the method limit of quantification (LOQ) of 0.01 ppm is recommended and is harmonized with Codex Maximum Residue Limit (MRL). The recent data also indicated that the current tolerance of 0.1 ppm for MCPA on pea hay and vines is too low. Tolerance levels of 0.60 ppm for pea vines and 1.5 ppm for pea hay are recommended.

HED has reviewed tolerances for grass, forage and grass, hay and has determined that current tolerances are too low. Upon review of the crop field trial study reflecting the use of MCPA on pasture and rangeland, grass showed residues of MCPA at preharvest intervals (PHIs) of 0, 7, 14, 21, and 30 days (MRID 45288704; Guideline 860.1500). In addition, the required variety of grasses were tested (bermuda, fescue, and brome) to establish a group tolerance. Using the OECD calculation procedure, the tolerance levels are 200 ppm for grass, forage and 400 ppm for grass, hay (Appendix C of D448530). To harmonize with Codex MRLs, HED recommends a tolerance of 500 ppm for grass, hay.

HED has reviewed tolerances for flax, wheat, grain and wheat, hay and has determined that current tolerances are too high. Upon review, crop field trial studies reflecting the use of MCPA on wheat showed residue levels that were lower than current tolerances (MRID 45763101; Guideline 860.1500). The study used exaggerated rates (2x label rate) of MCPA DMAS, MCPA 2-EHE, and MCPA NA on wheat crops in the United States. Using the OECD calculation procedure, the tolerance levels are 0.20 ppm for wheat, grain and 40 ppm for wheat, hay (Appendix C of D448530). To harmonize with Codex MRLs, HED recommends a tolerance of 50 ppm for wheat, hay. These values were translated to barley, oat, and rye crops based on previous translation decisions.

Flax crop field trial data (MRID 46242401; Guideline 860.1500) had been received and were reviewed by HED. The recent data indicated that the current tolerance of 0.1 ppm is too high. All samples collected were below the method limit of quantification (LOQ) of 0.025 ppm. To harmonize with Codex, HED recommends a tolerance of 0.01 ppm as more recent field trial data were available from Canada with a lower LOQ of 0.01 ppm and a higher application rate (2x U.S. field trial data). These data were reviewed in 2012 in the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) report number 257 for MCPA.

Hog and ruminant products and milk tolerances were updated based on new data received from the MCPA Task Force Three (MRID 47075201; Guideline 860.1480), and on the latest dietary burden calculations (See D448530, section 5.2.2.2 Estimated Secondary Residues in Livestock for more detailed information).

2.2.3 International Harmonization

Canada, Codex, and the U.S. have the same MCPA residue definition; residues of both free and conjugated MCPA are regulated (See Appendix C). There are currently no established MRLs from Codex or Canada for alfalfa, clover, lespedeza, trefoil, or vetch commodities. The U.S. tolerance level for meat (horse, sheep, cattle and goat) are harmonized with Codex MRLs. HED

recommends that the tolerance levels for milk and for livestock byproducts (horse, sheep, cattle and goat) fat and meat be revised to harmonize with Codex levels. HED also recommends that the tolerance levels for the following plant commodities be revised to harmonize with Codex levels: flax seed, dry peas, grass hay, and the forage, grain, hay, and straw of barley, oat, rye, and wheat.

2.3 Label Recommendations

2.3.1 Recommendations from Residue Reviews

HED recommends that the uses for direct application to alfalfa and clover be removed from the MCPA labels. Current tolerances listed for alfalfa and clover are based on residue data for the small grains underseeded uses (alfalfa and clover grown underneath a small grains crop), and do not reflect potential residues resulting from direct application to alfalfa and clover. There are no data supporting the direct application to alfalfa and clover (see data deficiencies outlined in Section 2.1).

2.3.2 Recommendations from Residential and Occupational Assessments

No specific label recommendations are being made, however, HED notes there are risk estimates of concern for several residential and occupational scenarios.

3.0 Introduction

3.1 Chemical Identity

Table 3.1. MCPA Nomenclature and Metabolite of Interest.

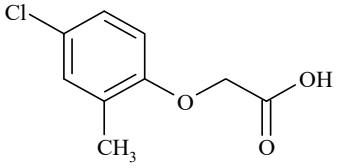
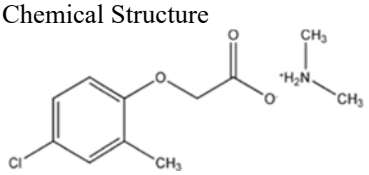
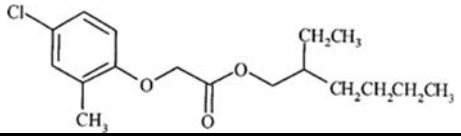
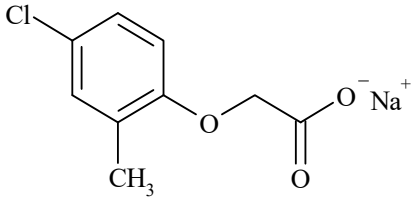
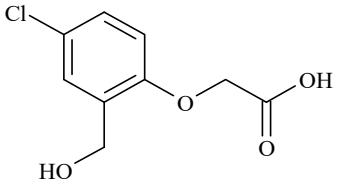
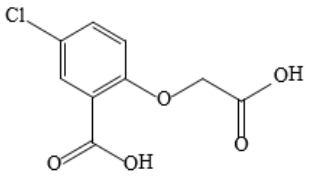
Compound	Chemical Structure 
Common name	**MCPA**
IUPAC name	4-chloro-o-tolyloxyacetic acid
CAS name	2-(4-chloro-2-methylphenoxy)acetic acid
CAS #	94-74-6
PC Code	030501
Compound	Chemical Structure 
Common name	**MCPA dimethylamine salt (DMA)**
IUPAC name	(4-chloro-2-methylphenoxy)acetic acid, dimethylamine salt

Table 3.1. MCPA Nomenclature and Metabolite of Interest.	
CAS name	(4-chloro-2-methylphenoxy)acetic acid, compound with N-methylmethanamine (1:1)
CAS #	2039-46-5
PC Code	030516
Compound	Chemical Structure 
Common name	**MCPA 2-ethylhexyl ester (2-EHE)**
IUPAC name	2-ethylhexyl 2-(4-chloro-2-methylphenoxy)acetate
CAS name	(4-chloro-2-methylphenoxy)acetic acid, 2-ethylhexyl ester
CAS #	29450-45-1
PC Code	030564
Compound	Chemical Structure 
Common name	**MCPA sodium salt (Na)**
IUPAC name	sodium 4-chloro-o-tolyloxyacetate
CAS name	sodium 2-(4-chloro-2-methylphenoxy)acetate
CAS #	3653-48-3
PC Code	030502
Metabolite	Chemical Structure 
Common name	**2-HMCPA**
IUPAC name	4-chloro-2-hydroxymethylphenoxyacetic acid
Metabolite	Chemical Structure 
Common name	**CCPA**
IUPAC name	2-carboxy-(4-chlorophenoxy)acetic acid
CAS name	2-carboxy-4-chlorophenoxyacetic acid

3.2 Physical/Chemical Characteristics

Appendix B summarizes the physical and chemical properties of MCPA, MCPA DMA and MCPA 2-EHE. No chemical identification information is available concerning the MCPA Na salt, except that it is water soluble. It is expected that this compound rapidly dissociates in an aqueous medium.

Both MCPA and MCPA DMA have low vapor pressure and significant exposure to these chemicals in the vapor phase is not expected. The octanol/water partitioning coefficient is also low, indicating that MCPA and MCPA DMA are unlikely to accumulate in fatty tissues. MCPA DMA rapidly dissociates in an aqueous medium to form the phenoxy moiety anion and the dimethyl ammonium ion. MCPA is practically insoluble in water.

MCPA 2-EHE has a low vapor pressure and significant exposure to the vapor phase is not expected. It has a high octanol/water partitioning coefficient and could potentially accumulate in fatty tissues. MCPA 2-EHE is practically insoluble in water.

MCPA DMA and MCPA 2-EHE will be rapidly converted to the free acid in the environment via dissociation (MCPA DMA), and hydrolysis and/or microbial degradation in soil (MCPA 2-EHE). MCPA is moderately stable in the environment and is mobile.

3.3 Pesticide Use Pattern

MCPA is registered for use on residential lawns, ornamental turf and trees, golf courses, parks, roadsides, rights of way; and for agricultural use on alfalfa, barley, clover, flax, oats, pasture and rangeland grass, peas, rye, triticale, wheat, and grass grown for seed. The end-use product formulations of MCPA include emulsifiable concentrates, soluble concentrates, liquids, granules, and ready-to-use (RTU) products. MCPA may be applied using aerial, groundboom, spreader or handheld equipment. Most, but not all, labels require baseline clothing (i.e., single layer clothing: long-sleeved shirt, long pants, shoes plus socks) and varying levels of additional personal protective equipment (PPE), such as respirators, chemical-resistant gloves, chemical-resistant aprons, coveralls (double layer), and chemical-resistant footwear. Additionally, the emulsifiable concentrate end-use products require the use of a closed-system (engineering controls- EC) when mixing and loading the product for aerial application. Restricted entry intervals (REIs) of 12 hours to 48 hours are listed on the registered labels.

The application rates of MCPA are summarized in the Line by Line, and Maximum Use Scenario Pesticide Label Usage Summary (PLUS) Reports as generated by OPP's Biological and Economic Analysis Division (BEAD).

3.4 Anticipated Exposure Pathways

MCPA is registered for use on several agricultural crops as well as on nonagricultural areas including ornamentals and turf (e.g., golf courses and residential lawns). Exposure to MCPA may occur from ingestion of residues in foods and in drinking water. There is the potential for dermal and inhalation exposure for adults (handlers) who mix and or apply MCPA. Exposure may also occur for adults (dermal) and children (dermal, incidental oral, episodic oral) who enter residential areas that have been previously treated with MCPA, such as lawns and golf courses.

In addition, there is the potential for exposure to spray drift from agricultural applications onto non-occupational sites such as lawns.

3.5 Consideration of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (http://www.archives.gov/federal-register/executive-orders/pdf/12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) and are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups, and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures are evaluated, based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application. Further considerations are currently in development, as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

4.0 Hazard Characterization and Dose-Response Assessment

MCPA is a member of the phenoxyacetic class of herbicides that function by mimicking the action of auxins, plant growth hormones. Formulations of MCPA are available in salt, ester, or amine forms. The active ingredients are MCPA (PC code 030501), MCPA sodium salt (PC code 030502), MCPA dimethylamine salt (MCPA DMA; PC code 030516), and MCPA 2-ethylhexyl ester (MCPA 2-EHE; PC code 030564). HIARC concluded that the toxicity of all forms of MCPA were essentially identical (TXR# 0052196, P. Chin, 10/29/2003).

4.1 Toxicology Studies Available for Analysis

The toxicology database on MCPA is complete and sufficient for assessing the toxicity and characterizing the hazard of MCPA. The toxicology studies for MCPA (including the acid, salt, ester and amine forms) are summarized in Appendix A. The database includes the following studies. An updated literature search was performed for MCPA and produced no studies that would impact the risk assessment (see Appendix E for the literature search sources, search parameters and number of articles identified).

- Subchronic: 21-day dermal toxicity (rabbit) – MCPA; 21-day dermal toxicity (rat) – MCPA DMA; 90-day oral toxicity (rat) – MCPA; 90-day oral toxicity (dog) – MCPA, MCPA DMA, MCPA 2-EHE; 28-day inhalation toxicity (rat) – MCPA, MCPA DMA
- Developmental toxicity: developmental toxicity (rat) – MCPA, MCPA DMA, MCPA 2-EHE; developmental toxicity (rabbit) – MCPA
- Reproduction: 2-generation reproduction study (rat) – MCPA
- Chronic: combined oral chronic toxicity/carcinogenicity (rat) – MCPA; carcinogenicity (mouse) – MCPA; chronic oral toxicity (dog) – MCPA
- Neurotoxicity: acute neurotoxicity (rat) – MCPA, MCPA DMA, MCPA 2-EHE subchronic neurotoxicity (rat) – MCPA, MCPA DMA, MCPA 2-EHE; developmental neurotoxicity (rat) – MCPA 2-EHE
- Other: mutagenicity battery - MCPA, MCPA DMA, MCPA 2-EHE
- Metabolism (rat) – MCPA, MCPA DMA, MCPA 2-EHE
- Dermal absorption - MCPA DMA, MCPA 2-EHE

HED's Hazard and Science Policy Committee (HASPOC) has recommended that the immunotoxicity testing be waived (TXR# 0056819, J. Leshin, 11/5/2013).

4.2 Absorption, Distribution, Metabolism, & Elimination (ADME)

A single gavage dose of 5 mg/kg or 100 mg/kg MCPA was rapidly absorbed, metabolized and eliminated in the urine (more than 85% within 12 hours) and feces (5%) in rats (MRIDs 43755201, 43755202, 43755203). Peak plasma concentrations in the rat were attained within 2 – 4 hours of dosing. No tissue accumulation was observed. The major components in the urine were MCPA (53-69%) and 4-chloro-2-hydroxymethyl-phenoxyacetic acid (HMCPA; 7-13%), an oxidation product of MCPA. The absorption and metabolism of MCPA DMA and MCPA 2-EHE in rats was similar to that of MCPA.

A single oral (gelatin capsules) dose of 5 mg/kg or 100 mg/kg MCPA was rapidly absorbed and metabolized, but slowly eliminated in the urine (58%) and feces (17%) in dogs (MRIDs 45595301, 45595302). Peak plasma concentrations in the dog were attained within 4.5 – 7 hours. The low overall recovery of radioactivity could be explained by prolonged renal clearance, which was still occurring at the 120-hour termination point. No tissue accumulation was observed. The major components in the urine were MCPA (14.5% of the dose), HMCPA (4.2%), a glycine conjugate of MCPA (28%), and a taurine conjugate of MCPA (9%). The major components in the feces were MCPA (8% of the dose), a glycine conjugate (3%), and a taurine conjugate (1%).

Based on data obtained from the open literature[1], the calculation of relevant pharmacokinetic parameters for MCPA in different species shows that renal clearance, volume of distribution, and plasma half-life of MCPA correlate with body weight (allometric scaling) for the rat and human,

[1] Timchalk, C. Toxicology 200 (2004), 1-19.

but not the dog (Figure 1 below). The longer plasma half-life, and slower elimination in the dog, results in substantially higher body burdens of MCPA, at comparable doses, relative to the rat and humans (Timchalk, 2004).

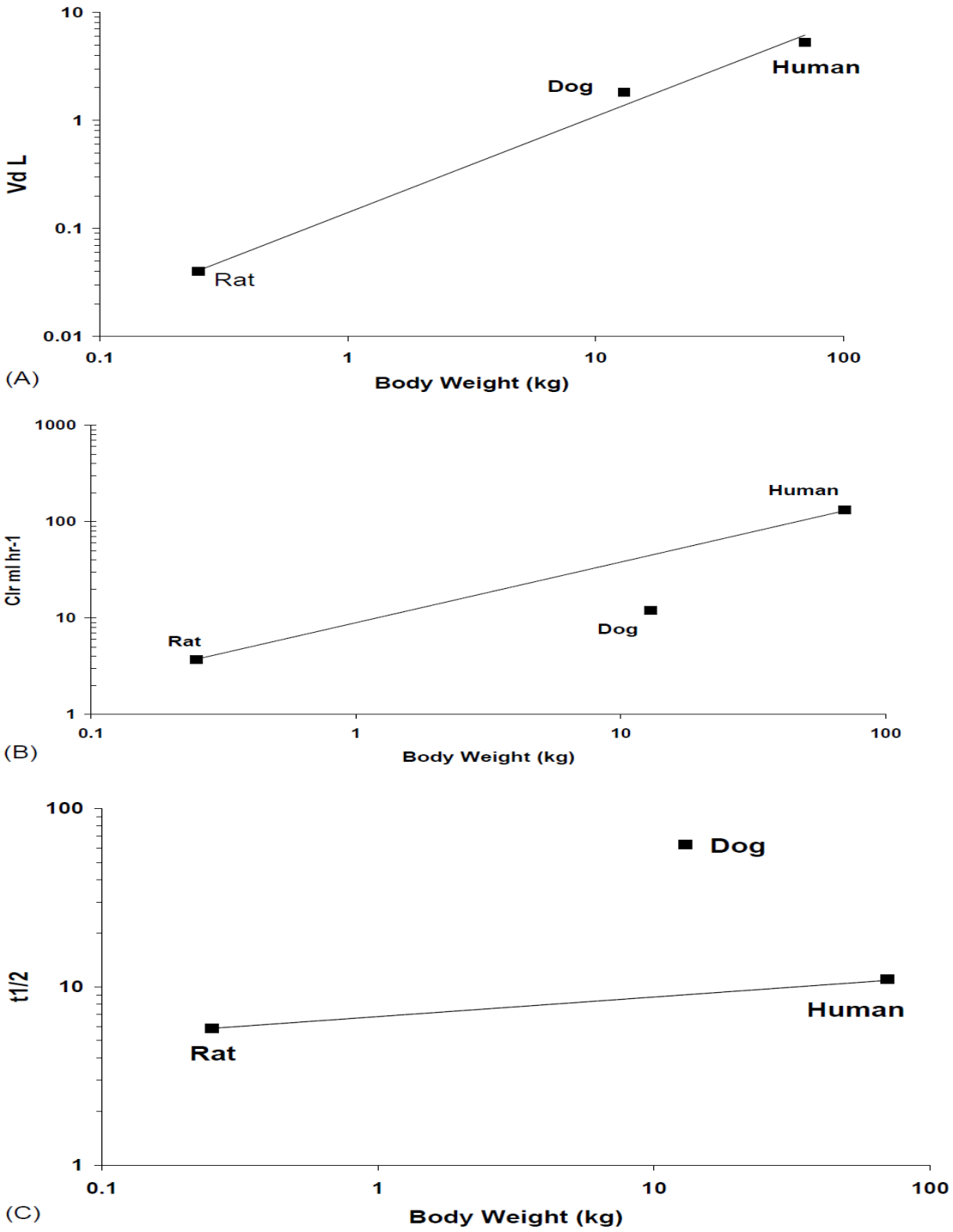


Figure 1. MCPA allometric relations between body weight and (A) volume of distribution (V_d) (all species); (B) renal clearance (Clr) (excluding dog); and (C) elimination half-life in hours ($t_{1/2}$) (excluding dog). From Timchalk, *Toxicology* 200 (2004), 1-19.

4.2.1 Dermal Absorption

The *in vivo* dermal absorption study in rats (2003; MRID 46327601) demonstrated a clear dermal absorption with time and dose. The results indicated dermal absorption factors (DAF) of 7.09% at 10 hours of exposure with the lowest dose tested (0.09 mg/cm^2), and 22.09% at the highest dose tested (7.5 mg/cm^2) based upon the sum of the excreta, cage wash, carcass, blood cells and plasma. The higher value of 22.09% is selected as the DAF for risk assessment. Although an *in vitro* dermal absorption study (MRID 45897010) using rat and human skin was available, it is not usable for risk assessment since it is not predictive of the dermal absorption pattern observed in the *in vivo* study. In the *in vivo* study, the highest dose (7.5 mg/cm^2) resulted in higher dermal absorption compared with the lowest dose tested (0.09 mg/cm^2). In contrast, an opposite pattern was noted in the *in vitro* study where the lowest dose tested (0.094 mg/cm^2) exhibited a higher dermal absorption than the highest dose tested (7.52 mg/cm^2).

4.3 Toxicological Effects

The kidney is the major target organ following oral exposure to MCPA. In rats, renal effects included increased creatinine levels, increased urea nitrogen levels, increased kidney weights, and increased chronic progressive nephropathy. In dogs, renal effects consisted of impaired renal function, increased urea nitrogen, increased creatinine levels, and increased pigmentation of the proximal tubular epithelium in the kidneys. Renal effects in rats occurred at lower doses in the chronic toxicity studies in comparison to subchronic toxicity studies indicating progression of toxicity over time. Renal hyperplasia has been observed in a chronic mouse study. Based on the kidney effects produced by MCPA from repeated dosing, the dog was shown to be much more sensitive than the rat. The increased sensitivity of dogs to MCPA was demonstrated to be a consequence of a reduced capacity to eliminate MCPA by dogs relative to rats and mice (see Section 4.2). Pharmacokinetic and interspecies allometric analyses of data reveal that the longer plasma half-life, and slower elimination in the dog, results in substantially higher body burdens of MCPA, at comparable doses, relative to the rat and humans (Timchalk, 2004)[1]. These analyses indicate that the dog is not an appropriate animal model for human health risk assessment. These findings are consistent with other phenoxyacetic acids such as 2,4-D (D442471, K. Lowe, 9/27/2017, 2,4-D – Revised Human Health Risk Assessment for Registration Review). Slight hepatotoxicity (increased liver enzyme levels) has also been observed in the chronic rat and chronic dog toxicity studies at a LOAEL associated with renal effects.

In a 21-day dermal rabbit study with MCPA acid, an increase in the incidence of mineralization in renal tubules was observed in both sexes at the limit dose (1000 mg/kg). There were dermal irritative effects at 100 mg/kg and 1000 mg/kg/day (erythema, desquamation, diffuse acanthosis, edema) and hyperkeratosis (1000 mg/kg/day). No evidence of systemic toxicity was apparent in a 21-day dermal rat study with MCPA-DMA; however, local irritative effects were noted at the limit dose.

MCPA is also considered to be a neurotoxicant based on clinical signs of neurotoxicity. Acute and subchronic neurotoxicity studies with MCPA, MCPA 2-EHE, and MCPA DMA in rats showed decreases in arousal, impairment of coordination (righting reflex) and gait, reduced motor activity, ataxia, and reduced hind grip strength. The developmental neurotoxicity study (DNT) in rats did not identify any concerns for developmental neurotoxicity in the pup.

In the subchronic inhalation toxicity studies with MCPA-DMA, respiratory tract effects were observed following repeat inhalation exposure. Respiratory tract effects included, bronchial/bronchiolar epithelial hypertrophy/hyperplasia, interstitial cell infiltration and peribronchiolar fibrogenesis, and increased lung weight. Nasal lesions included epithelial degeneration and goblet cell hypertrophy, but were not considered adverse based on severity scoring and lack of dose response.

Quantitative susceptibility was observed in the rat developmental toxicity study with MCPA acid based on increased incidence of skeletal retardation (incompletely ossified skulls, incompletely ossified or unossified sternebrae, dumbbell shaped thoracic vertebral bodies) and decreased fetal body weight at a dose that was a maternal NOAEL. There was also increased quantitative susceptibility in the two-generation rat reproductive toxicity study with MCPA acid as evidenced by decreased lactational pup body weight at an offspring LOAEL corresponding to a parental NOAEL. Qualitative susceptibility was noted in the developmental neurotoxicity (DNT) study with MCPA acid based on increased pup mortality and body weights at the same LOAEL as the maternal LOAEL (decreased body weight and food consumptions).

No treatment-related increase in tumor incidence in any MCPA treated groups when compared to controls was seen in the combined chronic/carcinogenicity study in rats and in carcinogenicity study in mice. MCPA has been classified as a "*Not Likely to Be Carcinogenic to Humans*" based on lack of evidence of carcinogenicity in rats and mice (HIARC; TXR# 0051862, P. Chin, 4/30/2003).

MCPA acid and MCPA DMA salt did not induce gene mutations in bacteria or mammalian cells *in vitro*. However, both MCPA acid and DMA salt induced structural chromosomal aberrations in cultured human lymphocytes *in vitro* in the presence, but not absence, of S9-activation. MCPA acid was also reported to be weakly positive for inducing sister chromatid exchanges (SCEs) in Chinese hamsters *in vivo* following a single dose of 1200 mg/kg; however, a follow-up study in Chinese hamsters tested up to 1200 mg/kg did not induce bone marrow chromosomal aberrations. Additionally, MCPA DMA salt was negative for the induction of micronuclei formation in bone marrow cells in mice. MCPA 2-EHE was negative for both gene mutations and chromosomal aberrations *in vitro*. Overall, there is low concern for mutagenicity *in vivo* for MCPA acid, MCPA DMA salt and MCPA 2-EHE.

MCPA is not acutely toxic by the oral (Toxicity Category III), dermal (Toxicity Category III), and inhalation (Toxicity Category IV) routes of exposure, based on lethality studies; it is not a skin irritant, but shows severe eye irritation and is negative for dermal sensitization. There is no concern for immunotoxicity, and the HASPOC recommended that the requirement for an immunotoxicity study be waived (TXR# 0056819, J. Leshin, 11/5/2013).

4.4 Safety Factor for Infants and Children (FQPA Safety Factor)[2]

HED recommends that the FQPA SF of 10X be reduced to 1X except for acute dietary and inhalation scenarios based on the following considerations: 1) the toxicity database is complete including adequate studies to assess the potential susceptibility in the young (including a developmental neurotoxicity study); 2) there is no indication of quantitative or qualitative susceptibility in the developmental toxicity studies in the rabbit; 3) clear NOAELs were identified for the quantitative susceptibility in the developmental toxicity study and two-generation reproductive study with MCPA in the rat; and 4) the endpoints and PoD chosen for risk assessment are protective of the susceptibility observed in the developmental and reproductive toxicity studies in the rat, and the developmental neurotoxicity study in the rat. Furthermore, the endpoints chosen for risk assessment are also protective of the potential neurotoxicity in all the ACN studies. The FQPA SF of 10X is retained for acute dietary (for the general population including infants and children) and inhalation scenarios for extrapolation of a LOAEL to a NOAEL.

4.4.1 Completeness of the Toxicology Database

The toxicology database for MCPA is complete. Acceptable rat and rabbit developmental toxicity studies, a rat 2-generation reproduction study, and acute, subchronic, and developmental neurotoxicity studies in rats are available.

4.4.2 Evidence of Neurotoxicity

Evidence of neurotoxicity was observed in the acute and subchronic neurotoxicity studies (MCPA, MCPA 2-EHE, and MCPA DMA) in rats, as indicated by various clinical signs of neurotoxicity (see Section 4.3). There were no developmental neurotoxic effects in the rat DNT study. There is a low degree of concern for the potential neurotoxic effects of MCPA since clear NOAELs were identified for the effects described above, there were no adverse neuropathological effects, and the endpoints chosen for risk assessment are protective of any potential neurotoxicity.

4.4.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

In the developmental rat study with MCPA acid, quantitative susceptibility was demonstrated based on increased incidence of skeletal retardation and decreased fetal body weight at a dose that was a maternal NOAEL (Section 4.3). MCPA acid, however, did not produce developmental toxicity in rabbits. Quantitative susceptibility was also evident in the two-generation reproduction study in rats with MCPA acid, in which lactational pup body weight decrements were noted at a dose in offspring that was a parental NOAEL (Section 4.3). Qualitative susceptibility was noted in the developmental neurotoxicity (DNT) study with MCPA acid based on increased pup mortality and body weights at the same LOAEL as the maternal LOAEL

[2] HED's standard toxicological, exposure, and risk assessment approaches are consistent with the requirements of EPA's children's environmental health policy (https://www.epa.gov/children/epas-policy-evaluating-risk-children).

(decreased body weight and food consumptions). There was no evidence of quantitative or qualitative susceptibility in the developmental rat studies with MCPA DMA and MCPA ester forms.

Considering the overall toxicity profile and the doses and endpoints selected for risk assessment, the degree of concern for the effects observed in the studies are low because the developmental/offspring effects observed in the studies are well characterized and clear NOAELs/LOAELs have been identified in the studies for the effects of concern. Additionally, the endpoints and PODs selected for risk assessment are protective of potential developmental/reproductive effects.

4.4.4 Residual Uncertainty in the Exposure Database

HED has used high-end assumptions in the dietary exposure assessment, including the use of 100% crop treated assumptions and tolerance-level residues, and upper-bound estimates of potential exposure through drinking water. In addition, the residential exposure assessment was conducted using chemical-specific data (where available) and HED's 2012 Residential SOPs[3]; as such, residential exposures are unlikely to be underestimated.

4.5 Toxicity Endpoint and Point of Departure Selections

Since the last risk assessment, NOAEL/LOAELs of those studies that were identified as potentially impacting endpoint selection were updated per current practices. Although certain NOAEL/LOAELs within the toxicity profile tables contain results that are no longer considered adverse based upon current practices (*e.g.* decreased body weight gain in the absence of decreased absolute body weight), NOAEL/LOAELs were not updated since the last risk assessment because it would not impact endpoint selection.

4.5.1 Dose-Response Assessment

Acute Dietary Exposure (general population including infants and children): The ACN study in the rat with MCPA DMA was selected to evaluate acute dietary risks for the general population including infants and children. It is appropriate for the route and duration of exposure and reflects a single-dose effect. The LOAEL of 142 mg/kg (acid equivalent and lowest tested dose) is based on ataxia in female rats. A NOAEL was not identified. Although an ACN study specific to MCPA acid was available, there was less confidence in the ACN MCPA acid study. There were differences in the LOAEL and NOAEL values with MCPA acid having a NOAEL (200 mg/kg) higher than the LOAELs for the DMA and EHE forms. This difference may be related to the timing when the measurements were taken among the various forms of MCPA. For the MCPA acid, measurements were taken at 24 hours, whereas measurements were taken at 30 minutes to 8 hours for MCPA DMA and at 2 to 8 hours for MCPA 2-EHE. The absorption and metabolic profiles for all forms of MCPA are similar suggesting that the time to peak effect would be similar among the various forms of MCPA. The longer time (24 hr) measurement for

[3] Available: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

MCPA in comparison to the shorter time measurements for the other 2 forms (DMA and EHE) indicates the MCPA study may have missed the time to peak effect. A total uncertainty factor (UF) of 1000 was applied to account for interspecies extrapolation (UF_A; 10X) and intraspecies variability (UF_H; 10X), and a 10X FQPA SF as a UF_L (for extrapolating a LOAEL to NOAEL). The aRfD and the aPAD = 0.142 mg/kg/day.

Acute Dietary Exposure (Females 13-49 yrs): The developmental rat study with MCPA 2-EHE was selected to evaluate acute dietary risks for females 13-49 years of age. It is appropriate for the route and duration of exposure and reflects a single-dose effect. The maternal LOAEL of 120 mg/kg/day (acid equivalent) was based on total litter resorptions (primarily early resorptions) and post-implantation loss. The maternal NOAEL was 40 mg/kg/day. A total UF of 100 was applied to account for interspecies extrapolation (10X) and intraspecies variability (10X), and FQPA SF (1X). The aRfD and the aPAD = 0.4 mg/kg/day

Chronic Dietary Exposure: The combined chronic toxicity/carcinogenicity study in rats with MCPA acid was selected as most appropriate for this scenario. The chronic dietary POD (NOAEL = 4.4 mg/kg/day) was based on nephrotoxicity (increase in retraction and granular surface of the kidney associated with an increase in chronic progressive nephropathy in males) in rats administered 17.6 mg/kg/day MCPA acid. A total UF of 100 was applied to account for interspecies extrapolation (10X) and intraspecies variability (10X), and FQPA SF (1X). The cRfD and cPAD = 0.044 mg/kg/day.

Incidental Oral (Short - and - Intermediate term): The two-generation reproduction toxicity study in the rat with MCPA acid was selected to evaluate short- and intermediate-term incidental oral exposure to infants and children. The offspring LOAEL of 22.5 mg/kg/day was based on decreased pup weights during lactation (offspring NOAEL = 7.5 mg/kg/day). The total UF is 100 based on 10X for interspecies extrapolation and 10X for intraspecies variability. The FQPA SF is 1X.

Short- and Intermediate-Term Dermal Endpoint: Although a route-specific study is available, the oral two-generation reproductive toxicity study in the rat was selected to ensure protection of the increased quantitative postnatal susceptibility (reproductive study) and quantitative susceptibility (developmental rat study) that is not assessed in the route specific study. The offspring LOAEL of 22.5 mg/kg/day was based on decreased pup weights during lactation (offspring NOAEL = 7.5 mg/kg/day). The total UF is 100 to account for interspecies extrapolation (10X) and intraspecies variability (10X). For residential dermal exposure the FQPA SF/UF is 1X. The DAF is 22%.

Short- and Intermediate-term Inhalation Endpoints: A route specific study (4-week inhalation toxicity with MCPA-DMA) in the rat was selected for this exposure scenario. The LOAEC was 0.01 mg/L based on histological effects in the respiratory tract effects (bronchial/bronchiolar hyperplasia/hypertrophy, interstitial cell infiltration and peribronchiolar fibrogenesis) and increased lung weights. A NOAEC was not identified. The LOAEC (0.01 mg/L) was converted to a human equivalent concentration (HEC) and human equivalent dose (HED) based on bronchial/bronchiolar effects utilizing the Agency's Reference Concentration (RfC) 1994 Methodology. HEC/HED values are summarized in Table 4.5.4.3. The total UF is 300 which

includes interspecies extrapolation (3X), intraspecies variability (10X), and either a 10X FQPA SF (residential uses) or 10x UF_L (occupational uses). The standard interspecies extrapolation uncertainty factor (UF_A) can be reduced from 10X to 3X because the calculation of human equivalent concentrations accounts for pharmacokinetic differences between human and the experimental species used in the selected study (rat). The PODs selected for risk assessment are protective of potential developmental/reproductive effects.

4.5.2 Recommendation for Combining Routes of Exposures for Risk Assessment

As part of conducting a human health risk assessment, HED considers risks from individual routes of exposure (oral, dermal, and inhalation). Based upon the same effects (decreased pup weight during lactation) observed in the selected endpoints for risk assessment, incidental oral and dermal routes of exposure can be combined. However, the inhalation exposure endpoint is based on respiratory tract effects, so the inhalation exposure cannot be combined with either oral or dermal exposures.

4.5.3 Cancer Classification and Risk Assessment Recommendation

In accordance with the Draft Guidelines for Carcinogen Risk Assessment (July 1999), the HIARC classified MCPA as "*Not Likely to Be Carcinogenic to Humans*". This classification is based on the lack of evidence of carcinogenicity in mice and rats. Overall, there is low concern for mutagenicity *in vivo* for MCPA acid, MCPA DMA salt and MCPA 2-EHE (see Section 4.3).

4.5.4 Summary of Points of Departure and Toxicity Endpoints Used in Human Risk Assessment

Toxicological doses/endpoints selected for the MCPA risk assessment are provided in Tables 4.5.4.1 and 4.5.4.2.

Table 4.5.4.1. Summary of Toxicological Doses and Endpoints for MCPA for Use in Dietary and Non-Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General Population) *(including episodic ingestion)*	LOAEL = 142 mg/kg (acid equivalent)	UF_A = 10x UF_H = 10x FQPA SF/UF_L = 10x	Acute RfD = 0.142 mg/kg/day aPAD = 0.142 mg/kg/day	Acute oral neurotoxicity in rats with MCPA DMA salt; MRID 43562702 (1994) LOAEL = 142 MCPA (acid mg/kg equivalent) (LDT) seen in female rats based on ataxia. NOAEL not established.

Table 4.5.4.1. Summary of Toxicological Doses and Endpoints for MCPA for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty/ FQPA Safety Factors**	**RfD, PAD, LOC for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary (Females 13-49 years)	NOAEL = 40 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF= 1x	Acute RfD = 0.4 mg/kg/day aPAD = 0.4 mg/kg/day	Developmental toxicity study (rats) MCPA-2-EHE 44954101 (1999) acceptable/guideline Maternal LOAEL = 120 mg/kg/day (as acid equivalent) based on total litter resorptions (primarily early resorptions) and post-implantation loss.
Chronic Dietary (All Populations)	NOAEL= 4.4 mg/kg/day	UFA= 10x UFH= 10x FQPA SF= 1x	Chronic RfD = 0.044 mg/kg/day cPAD = 0.044 mg/kg/day	Chronic toxicity/carcinogenicity study (rats) MCPA acid; MRID 40634101 (1988) LOAEL = 17.6 mg/kg/day based on nephrotoxicity (increase in retraction and granular surface of the kidney associated with an increase in chronic progressive nephropathy in males at 17.6 mg/kg/day.
Incidental Oral (Short- and Intermediate-Term)	Offspring toxicity NOAEL =7.5 mg/kg/day	UFA= 10x UFH= 10x FQPA SF= 1x	Residential LOC for MOE = 100	Two-generation repro rat study – MCPA acid; MRID 40041701 (1986) Offspring LOAEL =22.5 mg/kg/day based on decreased pup weights during lactation.
Dermal Short (1-30 days) and Intermediate (1-6 months) Term	Offspring toxicity NOAEL =7.5 mg/kg/day	UFA= 10x UFH= 10x FQPA SF= 1x	Residential LOC for MOE = 100 DAF = 22%	Two-generation repro rat study – MCPA acid; MRID 40041701 (1986) Offspring LOAEL =22.5 mg/kg/day based on decreased pup weights during lactation.
Inhalation Short (1-30 days) and Intermediate (1-6 months) Term	LOAEC = 0.01 mg/L (HEC/HED values in Table 4.5.4.3)	UFA= 3x UFH= 10x FQPA SF/UF_L=10x	LOC for MOE = 300	4-week inhalation toxicity study (rats); MCPA-DMA salt; MRID 48952902 (2012) LOAEC = 0.01 mg/L (acid equivalent) based on increased histological effects in the respiratory tract (bronchial/bronchiolar hyperplasia/hypertrophy, interstitial cell infiltration and peribronchiolar fibrogenesis) and increased lung weights. NOAEC not identified.
Cancer (all routes)	Classification: "*Not likely to be carcinogenic to humans*"			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate to a NOAEL. PAD =

population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. N/A = not applicable. DAF = dermal absorption factor (see Section 4.2.1)

Table 4.5.4.2. Summary of Toxicological Doses and Endpoints for MCPA for Use in Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal Short (1-30 days) and Intermediate (1-6 months) Term	Offspring toxicity NOAEL =7.5 mg/kg/day	UF_A= 10x UF_H= 10x	Occupational LOC for MOE = 100 DAF = 22%	Two-generation repro rat study – MCPA acid; MRID 40041701 (1986) Offspring LOAEL =22.5 mg/kg/day based on decreased pup weights during lactation
Inhalation Short (1-30 days) and Intermediate (1-6 months) Term	LOAEC = 0.01 mg/L (HEC/HED values in Table 4.5.4.3)	UF_A = 3x UF_H = 10x UF_L = 10x	Occupational LOC for MOE = 300	4-week inhalation toxicity study (rats) – MCPA-DMA salt; MRID 48952902 (2012) LOAEC = 0.01 mg/L(acid equivalent) based on histological effects (bronchial/bronchiolar hyperplasia/hypertrophy, interstitial cell infiltration and peribronchiolar fibrogenesis) and increased lung weight. NOAEC not identified.
Cancer (all routes)	Classification: "*Not likely to be carcinogenic to humans*"			

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). UF_L = use of a LOAEL to extrapolate to a NOAEL. MOE = margin of exposure. LOC = level of concern. N/A = not applicable. DAF = dermal absorption factor (see Section 4.2.1). HEC = human-equivalent concentration; HED = human-equivalent dose;

Table 4.5.4.3 Summary of HEC/HED Values for MCPA						
Population	**Scenario**	**Toxicity duration adjustment (Human Expected Exposure)**		**HEC**		**HED (mg/kg-day)**
		Daily	**Weekly**	**mg/L**	**mg/m^3**	
Occupational	Handler	0.75	1	0.032	32.138	3.041
Residential	Handler	NA	NA	0.043	42.850	1.014

Table 4.5.4.3 Summary of HEC/HED Values for MCPA						
Population	**Scenario**	**Toxicity duration adjustment (Human Expected Exposure)**		**HEC**		**HED (mg/kg-day)**
		Daily	**Weekly**	**mg/L**	**mg/m^3**	
	Outdoor post-application	NA	NA	0.043	42.850	1.166
	Indoor Post-application	NA	0.714	0.031	30.607	0.724
	Bystander	0.25	0.714	0.008	7.652	NA

HEC = human-equivalent concentration; HED = human-equivalent dose; HEC = rat POD × daily duration adjustment × weekly daily duration adjustment × RDDR (Regional Deposited Dose Ratio). HED = HEC × human-specific conversion factor (CF) × daily duration. Daily duration for the rat = 6 hrs; Daily exposure for humans (16 hrs for adults; 18 hrs for children); Animal weekly exposure = 5 days/week; human weekly exposure = 7 days/week CF = 13.8 L/min * 60 min/hr ÷ 70 kg; 13.8 L/min and 70 kg are default values within the RDDR.exe program. MMAD=0.59, GSD=2.65, RDDR (bronchiolar) = 4.285, Average male and female rat body weights = 261.6 g.

4.6 Endocrine Disruption

As required by FIFRA and the Federal Food, Drug, and Cosmetic Act (FFDCA), EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic, and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints that may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its reregistration decision for MCPA, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), MCPA is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a

chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[4] and includes some pesticides scheduled for Registration Review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[5]

5.0 Dietary Exposure and Risk Assessment

5.1 Metabolite/Degradate Residue Profile

The nature of the residue in plants and animals is adequately understood based on metabolism studies with wheat, goats, and hens. The primary residues found in plants are MCPA, and the metabolites 2-HMCPA [(4-chloro-2-hydroxymethylphenoxy)acetic acid] and CCPA [(4-chloro-2-carboxyphenoxy)acetic acid]. The primary residue in livestock commodities is MCPA.

In rats, MCPA was rapidly absorbed, metabolized and eliminated. No tissue accumulation was observed. The major component in the urine was MCPA, followed by lesser amounts of 2-HMCPA. The absorption and metabolism of MCPA DMA and MCPA 2-EHE in rats was similar to that of MCPA.

In dogs, MCPA was rapidly absorbed and metabolized but slowly eliminated (see Section 4.2). No tissue accumulation was observed. The major components in the urine were MCPA and a glycine conjugate of MCPA, with lesser amounts of 2-HMPCA and a taurine conjugate of MCPA. The major components in the feces were MCPA, a glycine conjugate, and a taurine conjugate.

5.1.1 Residues of Concern Summary and Rationale

HED's Metabolism Assessment Review Committee (D308991, C. Olinger, 10/7/2004) determined that there was insufficient information to conclude that the plant metabolite 2-

[4] See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
[5] http://www.epa.gov/endo/

HMCPA was significantly less toxic than MCPA; it is, therefore, included in the residue of concern in plants for risk assessment. It was concluded that the plant metabolite CCPA is significantly less toxic than MCPA; therefore, the risk contribution from the metabolite CCPA does not need to be included in MCPA assessments. Residues of MCPA will likely be equal to or exceed 2-HMCPA residues in plants, and therefore, MCPA would serve as a sufficient marker of misuse for tolerance enforcement. For livestock commodities, the residue of concern for tolerance enforcement is MCPA. For risk assessment, the residue of concern in livestock commodities and drinking water is MCPA.

The residues of concern for tolerance enforcement and risk assessment are presented in Table 5.1.1.

Table 5.1.1 Summary of Metabolites and Degradates to be included in the Risk Assessment and Tolerance Expression

Matrix		Residues included in Risk Assessment	Residues included in Tolerance Expression
Plants	Primary Crop	MCPA and 2-HMCPA	MCPA
	Rotational Crop	MCPA and 2-HMCPA	MCPA
Livestock	Ruminant	MCPA	MCPA
	Poultry	MCPA	MCPA
Drinking Water		MCPA	Not Applicable

5.2 Food Residue Profile

Residue chemistry data deficiencies have been identified and are summarized in section 2.1. Available data are adequate to assess MCPA on registered commodities with the exception of direct application on alfalfa and clover. Tolerances for residues of MCPA are established in 40 CFR 180.339 and range from 0.01 ppm (flax) to 500 ppm (grass, hay). Generally, residues below 0.20 ppm are expected in most food commodities except for ruminant meat byproducts (3.0 ppm). There is no expectation of finite residues in hog commodities, poultry commodities, and eggs. Processing studies have shown that concentration of residues is not expected to occur. There are no individual processed food commodity tolerances associated with the registered uses of MCPA. Residues of MCPA decline with increasing PHIs and have not been found in rotational crop studies at any plant back interval (PBI).

5.3 Water Residue Profile

The Environmental Fate and Effects Division (EFED) provided estimated drinking water concentrations (EDWCs) for the dietary risk assessments (D446322, I. Maher, 9/17/2018). The EDWCs are unrefined high-end estimates modeled using the Pesticide in Water Calculator (PWC).

Maximum EDWCs for MCPA in surface water and groundwater from use of MCPA simulated from grass and turf use at 1.5 lbs a.e./A twice per year at a 21-day interval are presented in Table 5.3. For groundwater sources of drinking water, the peak and post breakthrough average EDWCs for MCPA are 236 and 208 ppb respectively. For surface water sources of drinking water, the highest acute and 1-in-10-year annual average EDWCs associated with MCPA are 170 ppb and 16.4 ppb, respectively. The values used in the dietary assessment are from the modeled scenario that resulted in the highest EDWCs (groundwater; grass/turf scenario): 236 ppb for the acute assessment and 208 ppb for the chronic assessment. The EDWCs were entered into the dietary analyses as point estimates.

The drinking water models and their descriptions are available at the EPA internet site: Models for Pesticide Risk Assessment.

Table 5.3 Estimated Drinking Water Concentrations (EDWCs) for drinking water exposure assessment of MCPA[1].

Source of Drinking Water (Model)	MCPA residue concentration in drinking water (ppb)		
	Acute	**Chronic**	**Cancer Chronic**
Surface Water (PWC) PCA=1	Pastureland/rangeland[2]		
	170	16.4	6.97
	Grasses/Turf[3]		
	72.4	7.32	3.92
	Wheat[4]		
	38.2	2.93	1.56
Groundwater [5](PWC)	**236**	**208**	

[1] The highest EDWCs for evaluated use scenarios are shown in **bold**.
[2] Use pattern on pastureland/rangeland modeled with representative TXalfalfaOP scenario with two 1.5 lbs ae/A applications with 21-day interval. The highest acute EDWC is from the ground broadcast application, and the highest chronic and cancer chronic EDWCs are from the aerial application.
[3] Grasses/turf modeled with TNnurserySTD_V2 scenario with two applications of 1.5 lbs. ae/acre made in 21-day interval.
[4] Wheat modeled with TXwheatOP scenario and one application of 0.75 lbs ae/acre.
[5] EDWCs were generated for groundwater sources of drinking water using the Pesticides in Water Calculator (PWC) and GW Florida Citrus scenario simulated for grass/turf uses at 1.5 lbs ae/A applied twice per year with a 21-day retreatment interval.

The available surface water monitoring data in the STORET (STOrage and RETrieval) database reports the highest concentration of MCPA in surface water to be 45.8 ppb, while the groundwater monitoring data in the National Water Information System (NWIS) database reports the highest concentration to be 16.6 ppb. Surface monitoring data from major California urban areas indicates that MCPA was detected at a maximum of 13.59 ppb. The monitoring indicates that the chemical is more frequently detected in stormwater and transported with rain runoff into the receiving water, and less frequently detected during dry flow in surface water.

5.4 Dietary Risk Assessment

5.4.1 Description of Residue Data Used in Dietary Assessment

The acute and chronic dietary assessments are unrefined analyses based on tolerance-level residues. The residue of concern for tolerance enforcement for plants and livestock is the parent compound MCPA. For livestock, the residue of concern for the dietary assessment is the parent

compound MCPA only. However, for plants, the residues of concern for dietary assessment consists of MCPA and the metabolite 2-HMCA (D308991, C. Olinger, 10/7/2004). Data available reflecting the metabolites of MCPA in dry peas and flax seed are available and indicate that the sum of residues are less than the method LOQs (MRIDs 46242401 and 50107601). A metabolism study of MCPB on peas was translated to MCPA for peas (D442968, D. Nadrchal, 1/25/2018). However, these data had no detectable residues of the metabolite 2-HMCPA in pea seed. In commodities where the method LOQ was used (dry pea and flax seed) for setting the tolerance, a factor of 2x was applied to account for the residues of MCPA and 2-HMCPA. Residue inputs for dry peas and flax seed used 0.020 ppm.

In other commodities, the sum of MCPA and metabolite 2-HMCPA (and metabolite CCPA, which is not a residue of concern) are below tolerance levels in wheat, grain harvested at maturity in field trials conducted at an exaggerated rate (2x current label rate) (F. Fort, D307890, 09/14/2004). These wheat data have been translated to barley, oat, and rye commodities. The use of tolerance-level residues for all currently registered food uses is considered protective of the potential residues of parent MCPA and metabolite 2-HMCPA.

5.4.2 Percent Crop Treated Used in Dietary Assessment

A conservative assumption that 100 percent of the commodities in the assessment were treated (100% crop treated (CT)) was used in both the acute and chronic dietary exposure assessments.

5.4.3 Dietary Risk Estimates

The acute and chronic dietary (food and drinking water) exposure assessments for MCPA were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database, DEEM-FCID™, Version 3.16, which incorporates consumption data from USDA's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). This dietary survey was conducted from 2003 to 2008.

Dietary (food and drinking water) risk estimates are below 100% of the acute and chronic PADs and, therefore, are not of concern (Table 5.4.3). The acute risk estimates at the 95th percentile of exposure are 10% of the aPAD for the U.S. population, and 29% of the aPAD for infants (<1 year old) (the most highly exposed population subgroup).

The chronic dietary risk estimates are 12% of the cPAD for the U.S. population, and 28% of the cPAD for infants (the most highly exposed population subgroup).

As MCPA has been classified as "*Not Likely to Be Carcinogenic to Humans*," cancer risks were not assessed.

Table 5.4.3 Summary of Dietary (Food and Drinking Water) Exposure and Risk for MCPA.						
Population Subgroup	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	0.014124	10	0.005163	12	NA	NA
All Infants (<1 year old)*	**0.041232**	**29**	**0.012145**	**28**		
Children 1-2 years old	0.023604	17	0.009331	21		
Children 3-5 years old	0.018340	13	0.007485	17		
Children 6-12 years old	0.014331	10	0.005223	12		
Youth 13-19 years old	0.011679	8.2	0.003920	8.9		
Adults 20-49 years old	0.013370	9.4	0.004945	11		
Adults 50-99 years old	0.011920	8.4	0.004824	11		
Females 13-49 years old	0.013506	9.5	0.004882	11		

Bold entries are maximum exposure and risk estimates.

6.0 Residential (Non-Occupational) Exposure

Residential handler and post-application exposures are expected from the registered uses of MCPA in residential (non-occupational) areas. All residential scenarios were previously assessed; however, this assessment includes updates to HED's 2012 Residential SOPs along with policy changes for body weight assumptions.

6.1 Residential Handler Exposure/Risk Estimates

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are addressed somewhat differently by HED as homeowners are assumed to complete all elements of an application without use of any protective equipment.

Most registered MCPA product labels with residential use sites (e.g., lawns and garden and trees) require that handlers wear specific clothing (e.g., long sleeve shirt/long pants) and/or use PPE. Therefore, HED has made the assumption that these products are not for homeowner use, and has not conducted a quantitative residential handler assessment for those labels.

There are some registered MCPA product labels with residential use sites (e.g., lawns) that do not require specific clothing (e.g., long sleeve shirt/long pants) and/or PPE, and these labels have been considered in the residential handler assessment for MCPA.

The quantitative exposure/risk assessment developed for residential handlers is based on the following scenarios:

- Mixing/loading/applying liquids via hose-end sprayer

- Mixing/loading/applying liquids via manually-pressurized handwand
- Mixing/loading/applying liquids via sprinkler can
- Applying RTU via trigger spray bottle
- Applying RTU via hose-end sprayer
- Mixing/loading/applying liquids via backpack
- Mixing/loading/applying granules via push-type rotary spreader
- Mixing/loading/applying granules via belly grinder
- Mixing/loading/applying granules via spoon
- Mixing/loading/applying granules via cup
- Mixing/loading/applying via hand dispersal
- Mixing/loading/applying via shaker can

Residential Handler Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessments. Each assumption and factor is detailed below.

Application Rate: The application rates of MCPA are summarized in the Line by Line, and Maximum Use Scenario Pesticide Label Usage Summary (PLUS) Reports as generated by OPP's Biological and Economic Analysis Division (BEAD). Maximum application rates were used in this assessment.

Unit Exposures and Area Treated or Amount Handled: Unit exposure values and estimates for area treated or amount handled were taken from HED's 2012 Residential SOPs.

Exposure Duration: Residential handler exposure is expected to be short-term (1 to 30 days) in duration. Intermediate-term exposures are not likely because of the intermittent nature of applications by homeowners.

Combining Exposures/Risk Estimates

Inhalation and dermal exposures cannot be combined because those routes do not have a common toxicological endpoint.

Summary of Residential Handler Non-Cancer Exposure and Risk Estimates

The estimated residential handler dermal and inhalation risks are not of concern (i.e., MOEs are ≥ the dermal LOC = 100 and/or the inhalation LOC = 300). Dermal MOEs range from 260 to 10,000,000. Inhalation MOEs range from 5,200 to 2,600,000.

Table 6.1.1. Residential Handler Non-cancer Exposure and Risk Estimates for MCPA.									
Exposure Scenario	Level of Concern	Dermal Unit Exposure (mg/lb ae)[2]	Inhalation Unit Exposure (mg/lb ae)[2]	Maximum Application Rate[1]	Area Treated or Amount Handled Daily[2]	Dermal		Inhalation	
						Dose (mg/kg/day)[3]	MOE[4] (LOC = 100)	Dose (mg/kg/day)[5]	MOE[6] (LOC = 300)
Mixer/Loader/Applicator									
Liquids via Hose-end Sprayer 2217-954	100	13.4	0.022	0.92 lb ae/A	0.5 acres	0.017	440	0.00013	8,000
Liquids via Manually-pressurized Handwand 2217-954		63	0.018	0.01 lb ae/gallon	5 gallons	0.0087	870	0.000011	90,000
Liquids via Sprinkler Can 2217-954		13.4	0.022	0.000021 lb ae/ft^2	1000 ft^2	0.00077	9,700	0.0000058	180,000
RTU via Trigger Spray Bottle 2217-917		85.1	0.061	0.0045 lb ae/bottle	1 bottle	0.0011	7,100	0.0000034	300,000
RTU via Hose-end Sprayer 2217-954		6.26	0.034	0.92 lb ae/A	0.5 acres	0.0079	950	0.0002	5,200
Liquids via Backpack 2217-956		130	0.14	0.01 lb ae/gallon	5 gallons	0.018	420	0.000088	12,000
Granules via Push-type Rotary Spreader 2217-956		0.81	0.0026	1.05 lb ae/A	0.5 acres	0.0012	6,400	0.000017	59,000
Granules via Belly Grinder 2217-956		360	0.039	0.000024 lb ae/ft^2	1200 ft^2	0.029	260	0.000014	72,000

Table 6.1.1. Residential Handler Non-cancer Exposure and Risk Estimates for MCPA.									
Exposure Scenario	Level of Concern	Dermal Unit Exposure (mg/lb ae)[2]	Inhalation Unit Exposure (mg/lb ae)[2]	Maximum Application Rate[1]	Area Treated or Amount Handled Daily[2]	Dermal		Inhalation	
						Dose (mg/kg/day)[3]	MOE[4] (LOC = 100)	Dose (mg/kg/day)[5]	MOE[6] (LOC = 300)
Granules via Spoon 2217-956		6.2	0.087	0.000024 lb ae/ft^2	100 ft^2	0.000041	180,000	0.0000026	390,000
Granules via Cup 2217-956		0.11	0.013	0.000024 lb ae/ft^2	100 ft^2	0.00000073	10,000,000	0.00000039	2,600,000
Granules via Hand Dispersal 2217-956		160	0.38	0.000024 lb ae/ft^2	100 ft^2	0.0011	7,100	0.000011	89,000
Granules via Shaker Can 2217-956		0.11	0.013	0.000024 lb ae/ft^2	100 ft^2	0.00000073	10,000,000	0.00000039	2,600,000

1 Based on registered labels (EPA Reg. No. 2217-954, 2217-956, 2217-917).
2 Based on HED's 2012 Residential SOPs (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 Dermal Dose = Dermal Unit Exposure (mg/lb ae) × Application Rate (lb ae/acre or gal) × Area Treated or Amount Handled (A/day or gallons/day) × Dermal Absorption Factor (22%) ÷ Body Weight (80 kg).
4 Dermal MOE = Dermal POD (7.5 mg/kg/day) ÷ Dermal Dose (mg/kg/day).
5 Inhalation Dose = Inhalation Unit Exposure (mg/lb ae) × Application Rate (lb ae/acre or gal) × Area Treated or Amount Handled (A/day or gallons/day) ÷ BW (80 kg).
6 Inhalation MOE = Inhalation HED (1.014 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).
ae = acid equivalent

6.2 Residential Post-application Exposure/Risk Estimates

There is the potential for post-application exposure for individuals exposed as a result of being in an environment that has been previously treated with MCPA. The quantitative exposure/risk assessment for residential post-application exposures is based on dermal and incidental oral contact with turf following liquid or granule applications.

Ingestion of granules is considered an episodic event and not a routine behavior. Because HED does not believe that this would occur on a regular basis, our concern for human health is related to acute poisoning rather than short-term residue exposure. Therefore, the acute dietary point of departure is used to estimate risk resulting from episodic ingestion of granules.

The lifestages selected for each post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs. While not the only lifestage potentially exposed for these post-application scenarios, the lifestage that is included in the quantitative assessment is health protective for the exposures and risk estimates for any other potentially exposed lifestage.

Residential Post-application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential post-application risk assessment. Each assumption and factor is detailed in the 2012 Residential SOPs.

Ingestion Rate: The default ingestion rate for dry pesticide formulations (e.g., pellets and granules) is 0.3 gram/day for children 1 <2 years old. It is assumed that if 150 pounds of product were to be applied to a ½ acre lawn, the amount of product per square foot would be approximately 3 g/ft^2 and a child would consume in a day one-tenth of the product available in a square foot. According to the 2012 Residential SOPs, if product-specific information is available, the granular ingestion rate may be adjusted to reflect the amount of product applied on a per area basis if it is less or more than 150 pounds to a ½ acre lawn. For instance, if 50 pounds of product is meant to treat a ½ acre lawn, then the ingestion rate should be reduced by a third to 0.1 grams/day. The maximum application rate for MCPA on lawns is 1.85 lb ae/acre and the maximum percent of active ingredient in dry formulation is 1.4% (equivalent to 132 lb product/A or 66 lb product/0.5 A). Therefore, the point estimate for granular ingestion rate (GIgR) has been adjusted to 0.132 grams/day [(66 lb product/0.5 A * 0.3 grams/day)/150 lb product/0.5 A.

Application Rate: The application rates of MCPA are summarized in the Line by Line, and Maximum Use Scenario Pesticide Label Usage Summary (PLUS) Reports as generated by OPP's Biological and Economic Analysis Division (BEAD) and MCPA Maximum Application Rates Use Profile Spreadsheet. Maximum applications were used in this assessment.

Exposure Duration: Residential post-application exposures to treated turf are expected to be short-term in duration.

Turf Transferable Residues: Chemical-specific liquid TTR data have been submitted for MCPA. The TTR studies were reviewed and found to be acceptable for risk assessment. Details regarding the data can be found in D448528. The predicted Day 0 residue value of 0.251 µg/cm^2 from North Carolina Clean Crop MCP 4 Ester Herbicide (TRT4) was used to estimate residential post-application exposure and risk. The data are summarized below in Table 6.2.1. These data were used to assess post-application exposure to liquid formulations applied to turf. For granular formulations, default TTR values were used (i.e., 0.2% of the application rate is available on the day of application).

Table 6.2.1. Summary of TTR Values and Linear Regression Analysis Results for Treated Turf with MCPA.

Parameter	Clean Crop MCP 4 Ester Herbicide (TRT4)	Clean Crop MCP Amine 4 (TRT 5)
	North Carolina	North Carolina
Application Rate (lb ae/A) Target Appl. Rate = 1.5 lb ae/A	1.54	1.55
Measured Actual Average Day 0 (8-12 hour) Residue (µg/cm^2)	0.1908	0.2535
Predicted Day 0 Residue (µg/cm^2)	0.251	0.091
Slope	-0.741	-0.494
Half-life (days)	0.9	1.4
R^2	0.9387	0.7269

Note: Linear regression analysis based on DFRs collected after the third application.

Combining Exposure and Risk Estimates

Since dermal and incidental oral exposure routes share a common toxicological endpoint, risk estimates have been combined for those routes. The incidental oral scenarios (i.e., hand-to-mouth and object-to-mouth) should be considered inter-related and it is likely that they occur interspersed amongst each other across time. Combining both scenarios with the dermal exposure scenario would be overly-conservative because of the conservative nature of each individual assessment. Therefore, the post-application exposure scenarios that were combined for children 1 <2 years old are the dermal and hand-to-mouth scenarios. This combination is considered a protective estimate of children's exposure.

Summary of Residential Post-application Non-Cancer Exposure and Risk Estimates

Using the Day 0 predicted TTR values for liquid formulations and Day 0 default TTR assumptions for granular formulations, all residential post-application scenarios are not of concern (MOEs are greater than the LOC of 100), except exposures from high contact lawn activities for adults (on lawns treated with liquid formulations) and children (1 to <2 years old) (on lawns treated with liquid and granular formulations).

For adults, the dermal MOE resulting from high contact activity is 67 for liquid formulations. For children, the dermal MOE resulting from high contact activity is 34 for liquid formulations. The combined (dermal and incidental oral) MOEs for children resulting from high contact activity are 31 for liquid formulations and 85 for granules. The episodic granule ingestion scenario for children is of concern (MOE is less than the LOC of 1000) with an MOE of 860.

Use of Day 0 chemical-specific TTR values in the residential post-application assessment is considered a screening level, conservative approach. This approach has resulted in risk estimates of concern for high contact lawn activity scenarios for the liquid formulations. Therefore, HED has considered the modeled daily residue dissipation from the MCPA TTR liquid formulation data to further characterize residential post-application exposures to account for the conservative nature of the residential post-application turf assessment methodologies[6] for the scenarios that resulted in a MOE of concern.

Consistent with the 2012 Residential SOPs, HED has presented the exposures and risks estimated with Day 0 TTR data (Table 6.2.2), and upon further evaluation, HED has also conducted an assessment using an average TTR value that incorporates residues over the course of several days. The assessment uses the same conservative SOP inputs (i.e., high levels of contact, 1.5 hours daily exposure, 30 subsequent days of exposure, 14 hand-to-mouth events per hour with hand residues fully reloaded every fourth mouthing event), but assumes, in effect, an adult and/or child is exposed daily over the course of the exposure duration (i.e., 1 to 30 days for short-term exposure) to a residue equivalent to a multi-day average TTR, which takes into account dissipation of the chemical.

When considering a 6-day average, the short-term residential post-application risk estimates for high contact activities are not of concern for adults and children. The adult MOE is 220 and the child combined (dermal and incidental oral) MOE is 100.

Since the 6-day average TTR refinement resulted in a combined (dermal and incidental oral) MOE of 100, which is at the LOC, for children conducting high contact lawn activities, it is not possible to aggregate (combine) those exposures with dietary exposure as there is no room available in the 'risk cup' for any additional exposures. Therefore, for this scenario, HED has back-calculated the minimum number of days the TTR data would need to be averaged in order to reach an aggregate risk estimate that is not of concern. It was determined that an 8-day average TTR results in a combined (dermal and incidental oral) MOE of 120 for children (which results in an aggregate MOE of 110), and is not of concern.

Averaging TTR values over the duration of exposure is scientifically defensible since the risk assessment endpoint and point of departure for these scenarios is taken from a reproduction study which represent dosing of animals over many weeks. Therefore, averaging residential exposure over this time frame (by using average TTR values) is appropriate. While HED has determined that aggregate risks are acceptable using an 8-day averaging time, further refinements are possible since animals in the reproduction study were dosed for longer durations than 8 days.

Table 6.2.2 presents the residential post-application risk estimates for adults and children from exposure to treated turf.

[6] The conservatisms are discussed in the ORE assessment (D448528, U. Hassan, 9/27/2018).

Table 6.2.2. Residential Post-application Non-cancer Exposure and Risk Estimates for MCPA.								
Lifestage	**Post-application Exposure Scenario**		**Application Rate[1]**	**TTR**	**Dose (mg/kg/day)[2]**	**MOEs[3]**	**Combined Routes (included in Combined MOE)**	**Combined MOEs**
	Use Site	**Route of Exposure**						
Liquid Formulations								
Adults	High Contact Lawn Activities	Dermal	0.92 lb ae/A	Day 0	**0.11**	**67**		
				Day 0–6 Average	0.035	220		
				Day 0–8 Average	0.026	290		
	Mowing Turf			Day 0	0.0023	3,300		
	Golfing		1.39 lb ae/A		0.013	570		
Children 11 to < 16 years old	Mowing Turf		0.92 lb ae/A		0.0026	2,900		
	Golfing		1.39 lb ae/A		0.015	490		
Children 6 to <11 years old	Golfing				0.018	420		
Children 1 to <2 years old	High Contact Lawn Activities		0.92 lb ae/A		**0.22**	**34**	A	**Day 0 TTR (A) = 31** Day 0–6 Average TTR (B) = 100 Day 0–8 Average TTR (C) = 120
				Day 0–6 Average	0.069	110	B	
				Day 0–8 Average	0.052	140	C	
		Hand to Mouth		Day 0	0.021	370	A	
				Day 0–6 Average	0.0065	1,200	B	
				Day 0–8 Average	0.0048	1,600	C	
		Object to Mouth		Day 0	0.00062	12,000		
		Soil Ingestion		Day 0	0.000031	240,000		
Granular Formulations								
Adults	High Contact Lawn Activities	Dermal	1.85 lb ae/A	Day 0	0.035	210		

Table 6.2.2. Residential Post-application Non-cancer Exposure and Risk Estimates for MCPA.								
Lifestage	**Post-application Exposure Scenario**		**Application Rate[1]**	**TTR**	**Dose (mg/kg/day)[2]**	**MOEs[3]**	**Combined Routes (included in Combined MOE)**	**Combined MOEs**
	Use Site	**Route of Exposure**						
	Mowing Turf				0.00062	12000		
Children 11 to < 16 years old	Mowing Turf		1.05 lb ae/A		0.00071	11,000		
Children 1 to <2 years old	High Contact Lawn Activities		1.85 lb ae/A		0.067	110	X	**85** (granule)
		Hand to Mouth			0.021	370	X	
		Object to Mouth			0.0013	6000		
		Soil Ingestion			0.000063	120,000		
	Episodic Granule Ingestion	Oral	1.4% ai		0.16	860		

1 Based on BEAD PLUS Report.
2 Dose (mg/kg/day) algorithms provided in 2012 Residential SOPs (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 MOE = POD (7.5 mg/kg/day) ÷ Dose (mg/kg/day).
4 Combined MOE = 1 ÷ [(1/dermal MOE) + (1/inhalation MOE) + (1/incidental oral MOE)], where applicable.
Note : For episodic granule ingestion the dietary POD = 142 mg/kg/day with an LOC of 1000.

6.3 Residential Risk Estimates for Use in Aggregate Assessment

As identified in Section 6.2, some exposure scenarios on treated turf resulted in risk estimates of concern for adults and children. These exposure scenarios have not been considered for the purpose of performing an aggregate assessment since additional exposure from food and water would only increase the risk estimates. The scenarios that resulted in residential post-application risk estimates of concern are as follows:

- Adult dermal post-application exposure from high contact activities on lawns treated with liquid formulations using Day 0 TTR data
- Children (1 to <2 years old) combined (dermal plus incidental oral) post-application exposure from high contact activities on lawns treated with liquid or granular formulations using Day 0 TTR data (liquid – chemical specific TTR; and granule – default TTR)

Of the remaining residential exposure scenarios, only the most conservative, or worst case, residential adult and child scenarios have been selected to be included in the aggregate risk assessment. Table 6.3.1 reflects the residential risk estimates for use in the aggregate assessment for MCPA. Note that a recommendation has not been made for children 1 to <2 years old since scenarios for both the liquid and granular formulations result in risks of concern for that lifestage.

- The residential exposure for use in the adult aggregate assessment is dermal post-application exposure from high contact activities on lawns treated with granular formulations (Day 0 TTR)
- The residential exposure for use in the children 11 to <16 years old and children 6 to <11 years old aggregate assessments are dermal post-application exposures from golfing (Day 0 TTR).

Ingestion of granules is considered an episodic event and not a routine behavior. Because HED does not believe that this would occur on a regular basis, our concern for human health is related to acute poisoning rather than short-term residue exposure. Therefore, an acute dietary dose is used to estimate exposure and risk resulting from episodic ingestion of granules. For these same reasons, the episodic ingestion scenario is not recommended for inclusion in the aggregate assessment.

Table 6.3.1. Recommendations for the Residential Exposures for the MCPA Aggregate Assessment.

Lifestage	Exposure Scenario	Dose (mg/kg/day)[1]				MOE[2]			
		Dermal	Inhalation	Oral	Total	Dermal	Inhalation	Oral	Total
Adults	Post-application exposure from high contact activities on lawns treated with a granular formulation	0.035	N/A	N/A	0.035	210	N/A	N/A	210
Children 11 to <16 years old	Golfing (liquid formulation)	0.015	N/A	N/A	0.015	490	N/A	N/A	490
Children 6 to <11 years old	Golfing (liquid formulation)	0.018	N/A	N/A	0.018	420	N/A	N/A	420

1 Dose = the highest dose for each applicable lifestage of all residential scenarios assessed. Total = dermal + inhalation + incidental oral (where applicable).
2 MOE = the MOEs associated with the highest residential doses. Total = 1 ÷ (1/Dermal MOE) + (1/Inhalation MOE) + (1/Incidental Oral MOE), where applicable.

For the residential exposure scenarios with liquid formulations that resulted in risk estimates of concern when using Day 0 residues, recommendations for an aggregate assessment using the risk estimates resulting from refinement of the TTR values are also made (i.e., using 6- and 8-day average modeled TTR values). Table 6.3.2 reflects the residential risk estimates using the refined TTR data (6- and 8-day averages) for use in the aggregate assessment for MCPA.

Table 6.3.2. Residential Exposures for the MCPA Aggregate Assessment with Refinement (6- and 8-day Average TTR values).

Lifestage	Exposure Scenario	TTR Data	Dose (mg/kg/day)[1]				MOE[2]			
			Dermal	Inhalation	Oral	Total	Dermal	Inhalation	Oral	Total
Adults	High Contact Lawn Activities (liquid formulation)	Day 0-6	0.035	N/A	N/A	0.035	220	N/A	N/A	220
		Day 0-8	0.026	N/A	N/A	0.026	290	N/A	N/A	290
Children 1 to < 2 years old	High Contact Lawn Activities (liquid formulation)	Day 0-6	0.069	N/A	0.0065	0.076	110	N/A	1,200	100
		Day 0-8	0.052	N/A	0.0048	0.057	140	N/A	1,600	120

1 Dose = the highest dose for each applicable lifestage of all residential scenarios assessed. Total = dermal + inhalation + incidental oral (where applicable).
2 MOE = the MOEs associated with the highest residential doses. Total = 1 ÷ (1/Dermal MOE) + (1/Inhalation MOE) + (1/Incidental Oral MOE), where applicable.

7.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, HED must consider and aggregate (add) pesticide exposures and risks from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure. For MCPA, the appropriate durations of exposure for aggregate assessment are acute, short-term, and chronic. Since the short- and intermediate-term endpoints and PODs are the same, and short-term exposures are always higher than or equal to intermediate-term exposures, the short-term assessment is protective of any potential intermediate-term exposures.

7.1 Acute Aggregate Risk

Typically, HED does not consider residential exposures when assessing acute aggregate risk unless such exposures can be characterized as a series of single-day exposures, which is not the case for MCPA. Therefore, acute aggregate risk estimates for MCPA are equivalent to the acute dietary risk estimates (Section 5.4) and are below HED's level of concern.

7.2 Short- Term Aggregate Risk

In estimating the short-term aggregate risk for MCPA, HED has aggregated the short-term residential exposure (Table 6.3.1) and average dietary (food and water) exposure (Table 5.4.3). Residential exposure scenarios that resulted in risk estimates of concern (when using Day 0 TTR values) are not included in this aggregate assessment as combining those exposures with dietary exposures would result in even greater risk estimates of concern. The selected residential exposure scenarios for aggregation, adults conducting high contact lawn activities (granules) and children playing golf (liquid formulation), represent the worst-case risk estimates of the residential scenarios that were determined not to be of concern. Note that an aggregate assessmnt has not been conducted for children 1 to <2 years old since residential scenarios for both the liquid and granular formulations result in risks of concern.

For the scenarios assessed, the short-term aggregate MOEs for adults (190), children 6 to <11 years old (330), and children 11 to <16 years old (390) are above the LOC (100) and are not of concern.

Table 7.2.1 Short-Term Aggregate Risk Calculations (Day 0 TTR)

Population	Short- Term Scenario						
	NOAEL mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Food and Water Exposure mg/kg/day[3]	Residential Exposure mg/kg/day[4]	Total Exposure mg/kg/day[5]	Aggregate MOE (food, water, and residential)[6]
Adult ((High Contact Lawn activities/Granules)	7.5	100	0.075	0.004945	0.035	0.040	190
Children 11 to <16 years old (Golfer)	7.5	100	0.075	0.003920	0.015	0.019	390
Children 6 to <11 years old (Golfer)	7.5	100	0.075	0.005223	0.018	0.023	330

[1] LOC=100 (10X inter-species uncertainty factor and 10X intra- species uncertainty factor).

[2] Maximum Allowable Exposure (mg/kg/day) = NOAEL/LOC

[3] The adult dietary exposure used is for the population subgroup "Adults 20-49 years old" and is the highest exposure for any of the adult-only subgroups (Table 5.4.3). The children dietary exposure used in the MCPA aggregate assessment is that for "Children 6-12 years old" and "Youth 13-19 years old"(Table 5.4.3). For MCPA, the child lifestage with the highest dietary exposure (all infants) does not match the child lifestage for residential exposure being aggregated (children 6 to <11years old and children 11 to <16 years old). The lifestages selected for each residential post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs. This analysis provides a quantitative and qualitative basis for the representative lifestage for most residential post-application scenarios involving young children, as well as reasons why a residential assessment is not conducted for infants. For children, therefore, the MCPA aggregate assessment only combines the residential exposure estimates for children 6 to <11years old and, children 11 to <16 years old with the average dietary exposure estimates for the most similar lifestages (Children 6-12 years old and Youth 13-19 years old).

[4] Residential Exposure = [Dermal and Incidental oral exposure Exposure] (Table 6.3.1)

[5] Total Exposure =(Avg Food & Water Exposure + Residential Exposure)

[6] Aggregate MOE = [NOAEL / (Avg Food & Water Exposure + Residential Exposure)]

Short-term Aggregate Assessment with TTR Refinements

For the residential exposure scenarios with liquid formulations that resulted in risk estimates of concern (when using Day 0 chemical-specific TTR values), an aggregate assessment was performed incorporating the residential exposures estimated using the refinement of a 6-day average TTR. Those scenarios are adult and children, high contact activities on lawns treated with liquid formulations. Using 6-day average TTR, the short-term aggregate MOE for adults is 190 and is not of concern. However, the child MOE of 88 is below the LOC of 100 and is of concern.

Table 7.2.2 Short-Term Aggregate Risk Calculations (6-day Ave. TTR)

Population	Short- Term Scenario						
	NOAEL mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Food and Water Exposure mg/kg/day[3]	Residential Exposure mg/kg/day[4]	Total Exposure mg/kg/day[5]	Aggregate MOE (food, water, and residential)[6]
Adult (High Contact Lawn activities/Liquid)	7.5	100	0.075	0.004945	0.035	0.040	190
Children 1-2 years old (High Contact Lawn activities/Liquid)	7.5	100	0.075	0.009331	0.076	0.085	88

[1] LOC=100 (10X inter-species uncertainty factor and 10X intra- species uncertainty factor).

[2] Maximum Allowable Exposure (mg/kg/day) = NOAEL/LOC

[3] The adult dietary exposure used is for the population subgroup "Adults 20-49 years old" and is the highest exposure for any of the adult-only subgroups (Table 5.4.3). The children dietary exposure used in the MCPA aggregate assessment is that for "Children 1-2 years old" (Table 5.4.3). For MCPA, the child lifestage with the highest dietary exposure (all infants) does not match the child lifestage for residential exposure being aggregated (children 1 to <2 years old). The lifestages selected for each residential post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs. This analysis provides a quantitative and qualitative basis for the representative lifestage for most residential post-application scenarios involving young children, as well as reasons why a residential assessment is not conducted for infants. For children, therefore, the MCPA aggregate assessment only combines the residential exposure estimates for children 1 to <2 years old with the average dietary exposure estimates for the most similar lifestages (Children 1-2 years old).

[4] Residential Exposure = [Dermal and Incidental oral exposure Exposure] (Table 6.3.2)

[5] Total Exposure =(Avg Food & Water Exposure + Residential Exposure)

[6] Aggregate MOE = [NOAEL / (Avg Food & Water Exposure + Residential Exposure)]

For the residential exposure scenario that resulted in a risk estimate of concern when using the refined 6-day TTR average value (children high contact activities on lawns treated with liquid) HED has back-calculated the minimum number of days over which the TTR data would need to be averaged in order to result in an aggregate risk estimate that is not of concern. It was determined that a minimum 8-day average TTR results in an aggregate MOE above the LOC of 100. With the 8-day average TTR, the MOE for children is 110 and is not of concern.

Table 7.2.3 Short-Term Aggregate Risk Calculations (8-day Ave. TTR)							
Population	Short- Term Scenario						
	NOAEL mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Food and Water Exposure mg/kg/day[3]	Residential Exposure mg/kg/day[4]	Total Exposure mg/kg/day[5]	Aggregate MOE (food, water, and residential)[6]
Children 1-2 years old (High Contact Lawn activities/liquid)	7.5	100	0.075	0.009331	0.057	0.066	110

[1] LOC=100 (10X inter-species uncertainty factor and 10X intra- species uncertainty factor).
[2] Maximum Allowable Exposure (mg/kg/day) = NOAEL/LOC
[3] The children dietary exposure used in the MCPA aggregate assessment is that for "Children 1-2 years old" (Table 5.4.3). For MCPA, the child lifestage with the highest dietary exposure (all infants) does not match the child lifestage for residential exposure being aggregated (children 1 to <2 years old). The lifestages selected for each residential post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs. This analysis provides a quantitative and qualitative basis for the representative lifestage for most residential post-application scenarios involving young children, as well as reasons why a residential assessment is not conducted for infants. For children, therefore, the MCPA aggregate assessment only combines the residential exposure estimates for children 1 to <2 years old with the average dietary exposure estimates for the most similar lifestages (Children 1-2 years old).
[4] Residential Exposure = [Dermal and Incidental oral exposure Exposure] (Table 6.3.2)
[5] Total Exposure =(Avg Food & Water Exposure + Residential Exposure)
[6] Aggregate MOE = [NOAEL / (Avg Food & Water Exposure + Residential Exposure)]

7.3 Chronic Aggregate Risk

Chronic aggregate risk assessments address exposures that are likely to occur, continuously, for greater than six months. In the case of MCPA, residential exposures are not expected to occur on a chronic basis; therefore, the chronic aggregate risk estimates are equivalent to the dietary risk estimates (Section 5.4.3) and are below HED's level of concern.

7.4 Cancer Aggregate Risk

MCPA is classified as "*Not Likely to Be Carcinogenic to Humans*" therefore, a cancer assessment is not needed.

8.0 Non-Occupational Spray Drift Exposure and Risk Estimates

Off-target movement of pesticides can occur via many types of pathways and it is governed by a variety of factors. Sprays that are released and do not deposit in the application area end up off-target and can lead to exposures to those it may directly contact. They can also deposit on surfaces where contact with residues can eventually lead to indirect exposures (*e.g.*, children playing on lawns where residues have deposited next to treated fields). The potential risk estimates from these residues can be calculated using drift modeling onto 50 feet wide lawns coupled with methods employed for residential risk assessments for turf products.

The approach to be used for quantitatively incorporating spray drift into risk assessment is based on a premise of compliant applications which, by definition, should not result in direct exposures to individuals because of existing label language and other regulatory requirements intended to prevent them.[7] Direct exposures would include inhalation of the spray plume or being sprayed directly. Rather, the exposures addressed here are thought to occur indirectly through contact with impacted areas, such as residential lawns, when compliant applications are conducted. Given this premise, exposures for children (1 to 2 years old) and adults who have contact with turf where residues are assumed to have deposited via spray drift thus resulting in an indirect exposure, are the focus of this analysis analogous to how exposures to turf products are considered in risk assessment.

In order to evaluate the drift potential and associated risks, an approach based on drift modeling coupled with techniques used to evaluate residential uses of pesticides was utilized. Essentially, a residential turf assessment based on exposure to deposited residues has been completed to address drift from the agricultural applications of MCPA. In the spray drift scenario, the deposited residue value was determined based on the amount of spray drift that may occur at varying distances from the edge of the treated field using the AgDrift (v2.1.1) model and the *Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift Policy*. Once the deposited residue values were determined, the remainder of the spray drift assessment was based on the algorithms and input values specified in the (2012) *Standard Operating Procedures for Residential Risk Assessment (SOPs)*.

A screening approach was developed based on the use of the AgDrift model in situations where specific label guidance that defines application parameters is not available.[8] AgDrift is appropriate for use only when applications are made by aircraft, airblast orchard sprayers, and groundboom sprayers. When AgDrift was developed, a series of screening values (i.e., the Tier 1 option) were incorporated into the model and represent each equipment type and use under varied conditions. The screening options specifically recommended in this methodology were selected because they are plausible and represent a reasonable upper bound level of drift for common application methods in agriculture. These screening options are consistent with how spray drift is considered in a number of ecological risk assessments and in the process used to develop drinking water concentrations used for risk assessment. In all cases, each scenario is to be evaluated unless it is not plausible based on the anticipated use pattern (e.g., herbicides are not typically applied to tree canopies) or specific label prohibitions (e.g., aerial applications are not allowed). Section 8.1 provides the screening level drift related risk estimates.

In many cases, risks are of concern when the screening level estimates for spray drift are used as the basis for the analysis. In order to account for this issue and to provide additional risk management options additional spray drift deposition fractions were also considered. These drift estimates represent plausible options for pesticide labels.

[7] This approach is consistent with the requirements of the EPA's Worker Protection Standard.
[8] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#AgDrift

8.1 Combined Risk Estimates from Lawn Deposition Adjacent to Applications

The spray drift risk estimates are based on an estimated deposited residue concentration as a result of the screening level agricultural application scenarios. MCPA is used on alfalfa, barley, clover, flax, oats, pasture and rangeland grass, peas, rye, triticale, wheat, and grass grown for seed and can be applied via **groundboom and aerial** equipment. The recommended drift scenario screening level options are listed below:

- **Groundboom applications** are based on the AgDrift option for high boom height and using very fine to fine spray type using the 90th percentile results.

- **Aerial applications** are based on the use of AgDrift Tier 1 aerial option for a fine to medium spray type and a series of other parameters which will be described in more detail below (e.g., wind vector assumed to be 10 mph in a downwind direction for entire application/drift event).[9]

Dermal and incidental oral risk estimates were combined because the toxicity endpoint for each route of exposure is based on decreased pup weights during lactation in the 2-generation reproductive toxicity rat study. The total applicable LOC is 100 so MOEs < 100 would be of concern. For children (1 to <2 year old), dermal and incidental oral risk estimates from indirect exposure to MCPA related to spray drift were not of concern at the field edge. Adult dermal risk estimates from spray drift are not of concern at the field edge.

[9] AgDrift allows for consideration of even finer spray patterns characterized as very fine to fine. However, this spray pattern was not selected as the common screening basis since it is used less commonly for most agriculture.

Table 8.1.2. Adult Risk Estimates (MOEs) Related to Indirect Exposure to Spray Drift for MCPA for the Dermal Route of Exposure				
Crop/Rate Group	**Spray Type/ Nozzle Configuration**	**Appl. Rate (lb ae/A)**	**Estimated TTR (ug/cm^2)[a]**	**MOEs (LOC = 100)[b] At Edge**
Agricultural Premises/Areas				
Aerial	Fine to Medium	1.85	0.095	410
Groundboom	High Boom Very fine to Fine	2.79	0.14	380

a. Estimated TTR (ug/cm^2) = TTR residue data adjusted for the differences in the application rate.
b. MOEs at various distances from field edge = dermal MOEs. Dermal POD = 7.5 mg/kg/day. The dermal dose is calculated using the algorithms provided in the Turf Residential SOPs (http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide), and the TTR used in the calculations is the estimated TTR * drift fraction of spray drift that deposits on lawns at various distances from the field edge (see Appendix B.
c. The application rate of 1.85 lb ae/A for aerial applications and 2.79 lb ae/A for groundboom applications was from the BEAD PLUS Line by Line Report for agricultural premises/areas

Table 8.1.3. Children (1 to <2 years old) Risk Estimates (MOEs) Related to Indirect Exposure to Spray Drift for MCPA for the Combined Dermal and Oral Routes of Exposure				
Crop/Rate Group	**Spray Type/ Nozzle Configuration**	**Appl. Rate (lb ae/A)**	**Estimated TTR (ug/cm^2)[a]**	**MOEs (LOC = 100)[b] At Edge**
Agricultural Premises/Areas				
Aerial	Fine to Medium	1.85	0.095	190
Groundboom	High Boom Very fine to Fine	2.79	0.14	170

a. Estimated TTR (ug/cm^2) = TTR residue data adjusted for the differences in the application rate.
b. MOEs at various distances from field edge = combined dermal plus incidental oral MOEs. Dermal POD = 7.5 mg/kg/day and Incidental oral POD = 7.5 mg/kg/day. The dermal and incidental oral doses are calculated using the algorithms provided in the Turf Residential SOPs (http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide), and the TTR used in the calculations is the estimated TTR * drift fraction of spray drift that deposits on lawns at various distances from the field edge (see Appendix B.
c. The application rate of 1.85 lb ae/A for aerial applications and 2.79 lb ae/A for groundboom applications was from the BEAD PLUS Line by Line Report for agricultural premises/areas

9.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0687-0037). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for MCPA.

In addition to this screen, the Agency has developed a preliminary bystander volatilization inhalation exposure assessment for MCPA utilizing the currently available inhalation toxicity and air monitoring data.

There is an available air monitoring study conducted in California by the California Air Resources Board (CARB). The report presents the results of "real-time" air sampling (in San Luis Obispo County)[10]. However, the study was not utilized in this assessment, as air samples were taken while applications were being made, which is not representative of volatilization. If additional data are submitted, the Agency will conduct a preliminary bystander volatilization inhalation exposure assessment for MCPA.

10.0 Cumulative Exposure/Risk Characterization

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to MCPA and any other substances and MCPA does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that MCPA has a common mechanism of toxicity with other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* [https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework]. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs)[11] and

[10] https://www.cdpr.ca.gov/docs/emon/pubs/ehapreps/eh8601.pdf

[11] *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)

conducting cumulative risk assessments (CRA)[12]. During Registration Review, the agency will utilize this framework to determine if the available toxicological data for MCPA suggests a candidate CMG may be established with other pesticides. If a CMG is established, a screening-level toxicology and exposure analysis may be conducted to provide an initial screen for multiple pesticide exposure.

11.0 Occupational Exposure

11.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the registered uses. The quantitative exposure/risk assessment developed for occupational handlers is based on the scenarios listed in Table 11.1.1.

Occupational Handler Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor is detailed in table 11.1.1. on an individual basis.

Application Rate: The application rates of MCPA are summarized in the Line by Line, and Maximum Use Scenario Pesticide Label Usage Summary (PLUS) Reports as generated by OPP's Biological and Economic Analysis Division (BEAD) and MCPA Maximum Application Rates Use Profile Spreadsheet. Maximum applications rates were used in this assessment.

Unit Exposures: It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include Pesticide Handler Exposure Database (PHED) 1.1, the Agricultural Handler Exposure Task Force (AHETF) database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The

[12] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)

standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table[13]", which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at the Agency website[14].

Area Treated or Amount Handled: Each area treated or amount handled assumption is detailed in Table 11.1.1. on an individual basis and can be found in ExpoSAC Policy 9.1.

Exposure Duration: HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site. For most agricultural uses, it is reasonable to believe that occupational handlers will not apply the same chemical every day for more than a one-month time frame; however, there may be a large agribusiness and/or commercial applicators who may apply a product over a period of weeks (e.g., completing multiple applications for multiple clients within a region).

For MCPA, based on the registered uses, short- and intermediate-term and inhalation exposures are expected for occupational handlers.

Personal Protective Equipment: Estimates of dermal and inhalation exposure were calculated for various levels of personal protective equipment (PPE). Results are presented for "baseline," defined as a single layer of clothing consisting of a long-sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator, as well as baseline with various levels of PPE as necessary (e.g., gloves, respirator, etc). Most, but not all, labels require baseline clothing (i.e., single layer clothing: long-sleeved shirt, long pants, shoes plus socks) and varying levels of additional personal protective equipment (PPE), such as respirators, chemical-resistant gloves, chemical-resistant aprons, coveralls (double layer), and chemical-resistant footwear. Additionally, engineering controls on the emulsifiable concentrate (EC) end-use products require the use of a closed-system when mixing and loading the product for aerial application.

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates

Most occupational handler scenarios are not of concern (MOEs are greater than the LOC; dermal LOC = 100 and inhalation LOC = 300) with baseline PPE and engineering controls (for aerial applications) except:

- Mixing/loading liquids via mechanically pressurized handgun to rights-of-ways with a dermal MOE of 13;
- Mixing/loading liquids via groundboom to high-acreage field crops with a dermal MOE of 33;

[13] Available: https://www.epa.gov/sites/production/files/2018-06/documents/opp-hed-pesticide-handler-surrogate-unit-exposure-table-june-2018.pdf

[14] Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

- Applying spray via mechanically pressurized handgun to rights-of-way (e.g., utilities, railroad, roadways) with a dermal MOE of 7.5;
- Mixing/loading/applying liquids via backpack to landscaping, turf (lawns, athletic field, parks, etc.) with a dermal MOE of 59;
- Mixing/loading/applying liquids via manually-pressurized handwand to landscaping, turf (lawns, athletic field, parks, etc.) with a dermal MOE of 4.5;
- Mixing/loading/applying liquids via mechanically-pressurized handgun to landscaping, turf (lawns, athletic field, parks, etc.) with a dermal MOE of 6; and
- Mixing/loading/applying liquids via backpack to rights-of-way with a dermal MOE of 1.2 and an inhalation MOE of 89.

With the addition of various levels of PPE (i.e., gloves and double layer) the following scenarios were no longer of concern (MOEs are greater than the dermal LOC of 100):

- Mixing/loading/applying liquids via groundboom to high-acreage field crops using gloves results in a dermal MOE of 200;
- Mixing/loading/applying liquids via backpack to landscaping, turf (lawns, athletic field, parks, etc.) using gloves results in a dermal MOE of 120; and
- Mixing/loading/applying liquids via manually-pressurized handwand to landscaping, turf (lawns, athletic field, parks, etc.) using gloves results in a dermal MOE of 1,100.

The remaining scenarios listed above remain of concern for dermal exposures with the addition of maximum levels of PPE.

The Agency matches quantitative occupational exposure assessment with appropriate characterization of exposure potential. While HED presents quantitative risk estimates for human flaggers where appropriate, agricultural aviation has changed dramatically over the past two decades. According the 2012 National Agricultural Aviation Association (NAAA) survey of their membership, the use of GPS for swath guidance in agricultural aviation has grown steadily from the mid 1990's. Over the same time period, the use of human flaggers for aerial pesticide applications has decreased steadily from ~15% in the late 1990's to only 1% in the most recent (2012) NAAA survey. The Agency will continue to monitor all available information sources to best assess and characterize the exposure potential for human flaggers in agricultural aerial applications.

HED has no data to assess exposures to pilots using open cockpits. The only data available is for exposure to pilots in enclosed cockpits. Therefore, risks to pilots are assessed using the engineering control (enclosed cockpits) and baseline attire (long-sleeve shirt, long pants, shoes, and socks); per the Agency's Worker Protection Standard stipulations for engineering controls, pilots are not required to wear protective gloves for the duration of the application. With this level of protection, there are no risk estimates of concern for applicators.

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for MCPA.

Exposure Scenario EPA Reg. Nos.	Crop or Target	Dermal Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Inhalation Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Maximum Application Rate	App Rate Unit	Area Treated or Amount Handled Daily	Area Treated/ Amount Handled Unit	Dermal		Inhalation	
										Dose (mg/kg/day)	MOE	Dose (mg/kg/day)	MOE
Mixer/Loader													
Liquid, Backpack, Broadcast 228-395	Rights-of-way (e.g., utilities, railroad, roadways)	220	SL/No G	0.219	No-R	0.99	lb ae/gallon solution	1000	gallons solution	0.6	**13**	0.00271	1,100
		29.1	DL/G	0.219	No-R	0.99	lb ai/gallon solution	1000	gallons solution	0.0792	**95**	0.00271	1,100
Liquid, Mechanically-pressurized handgun, Broadcast 229-395		220	SL/No G	0.219	No-R	0.06	lb ae/gallon solution	1000	gallons solution	0.0363	210	0.000164	19,000
Granule, Tractor-drawn Spreader, Broadcast 228-324	Golf course (fairways, tees, greens)	23.6	SL/No G	0.825	No-R	1.39	lb ai/acre	40	acres	0.0036	2,100	0.000574	5,300
Granule, Tractor-drawn Spreader, Broadcast 228-324	Golf course (tees and greens only), landscaping, turf (lawns, athletic fields, parks, etc.)	23.6	SL/No G	0.825	No-R	1.85	lb ae/acre	5	acres	0.0006	1,300	0.0000954	32,000
Liquid, Aerial, Broadcast 62719-3	Sod, field crop, typical	8.6	EC	0.219	EC	1.5	lb ae/acre	350	acres	0.0124	600	0.000545	5,600
Liquid, Aerial, Broadcast 42750-14	Field crop, high-acreage	8.6	EC	0.219	EC	1.85	lb ae/acre	1200	acres	0.0525	140	0.0023	1,300
Liquid, Groundboom, Broadcast 228-267 42750-233	Golf course (tees and greens only), landscaping, turf (lawns, athletic fields, parks, etc.)	220	SL/No G	0.219	No-R	2.60	lb ae/acre	5	acres	0.00787	950	0.0000356	85,000
Liquid, Groundboom, Broadcast 228-267 42750-233	Golf course (fairways, tees, greens)	220	SL/No G	0.219	No-R	2.60	lb ae/acre	40	acres	0.063	120	0.000285	11,000
Liquid, Groundboom, Broadcast 62719-3	Sod, field crop, typical	220	SL/No G	0.219	No-R	1.5	lb ae/acre	80	acres	0.0726	100	0.000329	9,200

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for MCPA.

Exposure Scenario EPA Reg. Nos.	Crop or Target	Dermal Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Inhalation Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Maximum Application Rate	App Rate Unit	Area Treated or Amount Handled Daily	Area Treated/ Amount Handled Unit	Dermal		Inhalation	
										Dose (mg/kg/day)	MOE	Dose (mg/kg/day)	MOE
Liquid, Groundboom, Broadcast 228-199	Field crop, high-acreage	220	SL/No G	0.219	No-R	1.85	lb ai/acre	200	acres	0.224	**33**	0.00101	3000
		37.6	SL/G	0.219	No-R	1.85	lb ai/acre	200	acres	0.0382	200	0.00101	3000
Applicator													
Spray (all starting formulations), Aerial, Broadcast 62719-3	Sod, field crop, typical	2.08	EC	0.0049	EC	1.5	lb ae/acre	350	acres	0.003	2,500	0.0000321	95,000
Spray (all starting formulations), Aerial, Broadcast 42750-14	Field crop, high-acreage	2.08	EC	0.0049	EC	1.85	lb ae/acre	1200	acres	0.0127	590	0.000136	22,000
Spray (all starting formulations), Groundboom, Broadcast 228-267 42750-233	Golf course (tees and greens only), landscaping, turf (lawns, athletic fields, parks, etc.)	78.6	SL/No G	0.34	No-R	0.92	lb ae/acre	5	acres	0.00281	2,700	0.0000553	55,000
Spray (all starting formulations), Groundboom, Broadcast 228-267 42750-233	Golf course (fairways, tees, greens)	78.6	SL/No G	0.34	No-R	2.60	lb ae/acre	40	acres	0.0225	330	0.000443	6,900
Spray (all starting formulations), Groundboom, Broadcast 62719-3	Sod, field crop, typical	78.6	SL/No G	0.34	No-R	1.5	lb ae/acre	80	acres	0.0259	290	0.00051	6,000
Spray (all starting formulations),	Field crop, high-acreage	78.6	SL/No G	0.34	No-R	2.79	lb ae/acre	200	acres	0.0578	130	0.00153	2,000

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for MCPA.

Exposure Scenario EPA Reg. Nos.	Crop or Target	Dermal Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Inhalation Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Maximum Application Rate	App Rate Unit	Area Treated or Amount Handled Daily	Area Treated/ Amount Handled Unit	Dermal		Inhalation	
										Dose (mg/kg/day)	MOE	Dose (mg/kg/day)	MOE
Groundboom, Broadcast 228-199													
Spray (all starting formulations), Mechanically-pressurized Handgun, Broadcast 229-395	Rights-of-way (e.g., utilities, railroad, roadways)	6050	SL/No G	8.68	No-R	0.06	lb ae/gallon solution	1000	gallons solution	0.998	**7.5**	0.00651	470
		1360	DL/G							0.224	**33**	0.00651	470
Granule, Tractor-drawn Spreader, Broadcast 228-324	Golf course (fairways, tees, greens)	9.9	SL/No G	1.2	No-R	1.85	lb ae/acre	40	acres	0.00202	3,700	0.00111	2,700
Granule, Tractor-drawn Spreader, Broadcast 228-324	Golf course (tees and greens only), Landscaping, turf (lawns, athletic fields, parks, etc.)	9.9	SL/No G	1.2	No-R	1.85	lb ae/acre	5	acres	0.000252	30,000	0.000139	22,000
Liquid, Trigger-spray bottle, Broadcast 2217-917	Exterior Building Components (e.g., foundations, perimeters, door/window frames, etc.); Landscaping, plants/flowers; Landscaping, turf (lawns, athletic fields, parks, etc.)	3660	SL/No G	61.2	No-R	0.023	lb ae/bottle	10	bottles	0.00235	3,200	0.000179	17,000
Flagger													
Spray (all starting formulations), Aerial, Broadcast 62719-3	Sod, field crop, typical	11	SL/No G	0.35	No-R	1.5	lb ae/acre	350	acres	0.0159	470	0.0023	1,300
Spray (all starting formulations), Aerial, Broadcast	Field crop, high acreage					1.85				0.0196	380	0.00284	1,100

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for MCPA.

Exposure Scenario EPA Reg. Nos.	Crop or Target	Dermal Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Inhalation Unit Exposure (µg/lb ae)	Level of PPE or Engineering control	Maximum Application Rate	App Rate Unit	Area Treated or Amount Handled Daily	Area Treated/ Amount Handled Unit	Dermal		Inhalation	
										Dose (mg/kg/day)	MOE	Dose (mg/kg/day)	MOE
42750-14													
Mixer/Loader/Applicator													
Liquid, Backpack, Broadcast 11685-21	Landscaping, turf (lawns, athletic fields, parks, etc.)	58400	SL/No G	69.1	No-R	0.14	lb ai/gallon solution	40	gallons solution	0.127	**59**	0.00018	17,000
		16900	DL/G	69.1	No-R	0.14	lb ai/gallon solution	40	gallons solution	0.0635	120	0.00018	17,000
Liquid, Manually-pressurized Handwand, Broadcast 62719-13	Landscaping, turf (lawns, athletic fields, parks, etc.)	100000	SL/No G	30	No-R	0.15	lb ai/gallon solution	40	gallons solution	1.65	**4.5**	0.00225	1,400
		430	SL/G	30	No-R	0.15	lb ai/gallon solution	40	gallons solution	0.0071	1,100	0.00225	1,400
Liquid, Mechanically-pressurized Handgun, Broadcast 2217-966	Landscaping, turf (lawns, athletic fields, parks, etc.); Field crop, typical	6050	SL/No G	8.68	No-R	0.075	lb ai/gallon solution	1000	gallons solution	1.25	**6**	0.00814	370
		1360	DL/G	8.68	No-R	0.075	lb ai/gallon solution	1000	gallons solution	0.281	**27**	0.00814	370
Liquid, Mechanically-pressurized Handgun, Broadcast 228-267 42750-233	Golf course (fairways, tees, and greens)	1140	SL/No G	1.9	No-R	2.60	lb ae/acre	5	acres	0.0407	180	0.000309	9,800
Loader/Applicator													
Liquid, Backpack, Broadcast 228-395	Rights-of-way (e.g., utilities, railroad, roadways)	58400	SL/No G	69.1	No-R	0.99	lb ae/gallon solution	40	gallons solution	6.35	**1.2**	0.0343	**89**
		16900	DL/G	6.91	PF10 R	0.99	lb ae/gallon solution	40	gallons solution	1.84	**4.1**	0.00343	890
Granule, Belly grinder, Broadcast 228-324	Landscaping, turf (lawns, athletic fields, parks, etc.)	10000	SL/No G	62	No-R	1.85	lb ae/acre	1	acres	0.0509	150	0.00144	2,100
Granule, Rotary spreader, Broadcast 228-324	Golf course (fairways, tees, and greens only); Landscaping, turf	440	SL/No G	10	No-R	1.85	lb ae/acre	5	acres	0.0112	670	0.00116	2,600

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for MCPA.													
Exposure Scenario EPA Reg. Nos.	**Crop or Target**	**Dermal Unit Exposure (µg/lb ae)**	**Level of PPE or Engineering control**	**Inhalation Unit Exposure (µg/lb ae)**	**Level of PPE or Engineering control**	**Maximum Application Rate**	**App Rate Unit**	**Area Treated or Amount Handled Daily**	**Area Treated/ Amount Handled Unit**	**Dermal**		**Inhalation**	
										Dose (mg/kg/day)	**MOE**	**Dose (mg/kg/day)**	**MOE**
	(lawns, athletic fields, parks, etc.)												

1 Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data); Level of mitigation: Baseline, PPE, Eng. Controls.
2 Based on BEAD Line by Line Plus Report, Use Profile Spreadsheet, and additional information provided on relevant labels.
3 Exposure Science Advisory Council Policy #9.1.
4 Dermal Dose = Dermal Unit Exposure (µg/lb ae) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ae/acre or gal) × Area Treated or Amount Handled Daily (A or gal/day) × DAF (22 %) ÷ BW (80 kg).
5 Dermal MOE = Dermal POD (7.5 mg/kg/day) ÷ Dermal Dose (mg/kg/day).
6 Inhalation Dose = Inhalation Unit Exposure (µg/lb ae) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ae/acre or gal) × Area Treated or Amount Handled Daily (A or gal/day) ÷ BW (80 kg).
7 Inhalation MOE = Inhalation HED (3.041 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

11.2 Occupational Post-application Exposure/Risk Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

11.2.1 Occupational Post-application Inhalation Exposure/Risk Estimates

There are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0687-0037). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (https://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for MCPA.

In addition, the Agency is continuing to evaluate the available post-application inhalation exposure data generated by the Agricultural Reentry Task Force. Given these two efforts, the Agency will continue to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments.

11.2.2 Occupational Post-application Dermal Exposure/Risk Estimates

Occupational Post-application Dermal Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the occupational post-application risk assessments. Each assumption and factor is detailed below on an individual basis.

Exposure Duration: HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. For MCPA, based on the registered uses, short- and intermediate-term exposures are expected.

Transfer Coefficients: It is the policy of HED to use the best available data to assess post-application exposure. Sources of generic post-application data, used as surrogate data in the absence of chemical-specific data, are derived from Agricultural Reentry Task Force (ARTF)

exposure monitoring studies, and, as proprietary data, are subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting post-application exposure that are used in this assessment, known as "transfer coefficients", are presented in the ExpoSAC Policy 3[15]" which, along with additional information about the ARTF data, can be found at the Agency website[16]. Table 11.2.2.1 provides a summary of the anticipated post-application activities and associated transfer coefficients for the registered crops/use sites.

Application Rate: The application rates of MCPA are summarized in the Line by Line, and Maximum Use Scenario Pesticide Label Usage Summary (PLUS) Reports as generated by OPP's Biological and Economic Analysis Division (BEAD). Maximum application rates were used in this assessment.

Exposure Time: The average occupational workday is assumed to be 8 hours.

Dislodgeable Foliar Residues: In accordance with 40 CFR 158, DFR data are required for all occupational (e.g., crop, nursery, greenhouse use sites) or residential (e.g., ornamental and vegetable gardens, pick your own farms, retail tree farms) uses that could result in post-application exposure to foliage. In the absence of chemical-specific DFR data, EPA uses default values. Chemical-specific DFR data (Guideline 875.2100) are not available for MCPA (these data were originally requested in HED's memorandum *MCPA Human Health Risk Assessment Scoping Document in Support of Registration Review*, D414988, A. LaMay, 2/6/2014). Therefore, this assessment uses HED's default assumption that 25% of the application is available for transfer on day 0 following the application and the residues dissipate at a rate of 10% each following day. Since the highest estimated occupational post-application exposure using default DFR values for MCPA is not minimal in comparison to the level of concern (i.e., the calculated MOE is not greater than 2 times higher than the level of concern, MOE = 100 (DAT5) compared to the LOC of 100), these 40 CFR 158 DFR data should be submitted. The DFR data will facilitate any necessary exposure assessment refinements and will further EPA's general understanding of the availability of dislodgeable foliar pesticide residues.

Chemical-specific TTR data have been submitted for MCPA as described above in Section 6.2. TTR data were used for sod and golf course post-application risk estimates.

Occupational Post-application Non-Cancer Dermal Risk Estimates

All occupational post-application scenarios are not of concern (MOEs > LOC; dermal LOC = 100) except irrigation (handset) for forage crop, which is no longer of concern on DAT11 and scouting for forage crop, which is no longer of concern on DAT5.

[15] Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

[16] Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

Table 11.2.2.1. Occupational Post-application Non-Cancer Exposure and Risk Estimates for MCPA.					
Crop/Site	**Activities**	**Transfer Coefficient (cm^2/hr)**	**TTR/DFR (µg/cm^2)[1]**	**Dermal Dose (mg/kg/day)[2]**	**MOE[3] (LOC = 100)**
Short-term					
Sod	Maintenance, Slab Harvesting, Transplanting/Planting	6700	TTR = 0.24 at Day 0	0.036	210
Golf Course	Maintenance	3700	TTR = 0.42 at Day 0	0.034	220
	Maintenance (greens only)	2500		0.023	320
Alfalfa	Irrigation (handset)	1900	DFR = 1.40 at Day 0	0.059	130
Forage Crop			DFR = 1.63 at Day 11	0.068	110 (DAT11)
Pea, green			DFR = 1.05 at Day 0	0.0044	170
Alfalfa	Scouting	1100	DFR = 1.40 at Day 0	0.034	220
Barley			DFR = 2.15 at Day 0	0.052	140
Flax			DFR = 0.70 at Day 0	0.017	440
Forage Crop			DFR = 3.06 at Day 5	0.126	100 (DAT5)
Pea, Green	Harvesting, Hand		DFR = 1.05 at Day 0	0.025	290
Wheat, spring	Scouting		DFR = 2.15 at Day 0	0.052	140
Wheat, winter			DFR = 2.15 at Day 0	0.052	140
Pea, Green	Weeding, Hand	70	DFR = 1.05 at Day 0	0.002	4600
Wheat, Spring			DFR = 2.15 at Day 0	0.003	2300

1 TTR = predicted Day 0 residue value from study (0.251 µg/cm^2) adjusted for difference in application rate: 1.5 lb ae/A for sod and 2.6 lb ae/A for golf course. DFR = Application Rate (lb ae/A) × F × $(1-D)^t$ × 4.54E8 µg/lb × 2.47E-8 acre/cm^2; where F = 0.25 and D = 0.10 per day for the other crops/sites.

2 Daily Dermal Dose = [DFR or TTR (µg/cm^2) × Transfer Coefficient (cm^2/hr) × 0.001 mg/µg × 8 hrs/day × dermal absorption (22 %)] ÷ BW (80 kg).

3 MOE = POD (7.5 mg/kg/day) / Daily Dermal Dose. MOEs at Day 0 except when noted.

Restricted Entry Interval

Formulations of MCPA are available in salt, ester, or amine forms. MCPA acid and MCPA 2-EHE are classified as Toxicity Category IV via the dermal route and Toxicity Category IV for skin irritation potential. They are not skin sensitizers. MCPA amine and MCPA Na salt are classified as Toxicity Category III and IV, respectively, via the dermal route and Toxicity Category IV for skin irritation. They are not skin sensitizers. MCPA acid and MCPA amine are classified as category I for eye irritation and MCPA Na salt is classified as Toxicity Category II for eye irritation. Under 40 CFR 156.208 (c) (2), ai's classified as Acute I or II for acute dermal, eye irritation or primary skin irritation are assigned a 48- or 24-hour REI, respectively. Acute toxicity categories of III or IV are assigned a 12-hour REI. Short- and intermediate-term post-application risk estimates were not a

concern on day 0 (12 hours following application) for most activities; however, there were risk estimates of concern related to handset irrigation and scouting for forage crops.

Restricted entry intervals (REIs) of 12 hours to 48 hours are listed on the registered labels. Any changes to the REIs should take into consideration the post-application assessment, as well as any acute toxicity concerns for eye irritation.

12.0 Incident and Epidemiological Data Review

MCPA incidents were previously reviewed in 2013 (S. Recore and E. Evans, D415940, 12/3/13). At that time, based on the low severity and frequency of cases reported to both the Incident Data System (IDS) and the Centers for Disease Control and Prevention (CDC)/National Institute for Occupational Safety and Health (NIOSH) Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides, there was not a risk of concern that warranted further analysis.

HED performed an updated Tier I review of human incidents for MCPA using the OPP IDS and the CDC/NIOSH SENSOR databases (S. Recore and E. Evans, D448531, 8/23/2018).

In the current five-year IDS analysis from January 1, 2013 to August 7, 2018, no incidents involving a single active ingredient, and 25 incidents involving multiple active ingredients were reported to Main IDS. Two incidents were classified as major severity, and 23 incidents were classified as moderate severity. For Aggregate IDS, for the same five-year period, there were 132 incidents reported involving MCPA. These incidents were classified as minor severity.

A query of SENSOR-Pesticides from 2010-2014 identified 27 cases involving MCPA. All 27 cases were low in severity. One case involved a single active ingredient and 26 cases involved multiple active ingredients. Twelve cases were occupational and 15 cases were non-occupational. Symptoms frequently reported included: headache, eye pain/irritation, dizziness, vomiting, stomach cramps, skin redness, and skin pain.

The Agricultural Health Study (AHS) is a federally-funded study that evaluates associations between pesticide exposures and cancer and other health outcomes and represents a collaborative effort between the US National Cancer Institute (NCI), National Institute of Environmental Health Sciences (NIEHS), CDC's National Institute of Occupational Safety and Health (NIOSH), and the US EPA. MCPA is not included in the AHS, and, therefore, this study does not provide information for this report.

Based on the continued low frequency and mostly low severity of MCPA incidents reported to both IDS and SENSOR-Pesticides, there does not appear to be a concern at this time.

13.0 References

U. Hassan, 9/27/2018, MCPA. Occupational and Residential Exposure Assessment for the Registration Review of MCPA, D448528.

I. Maher, 9/17/2018, MCPA and salts and esters – Registration Review Drinking Water Assessment, D446322.

D. Nadrchal, 9/27/2018, MCPA. Registration Review. Summary of Analytical Chemistry and Residue Data, D448530.

D. Nadrchal, 9/27/2018, MCPA**.** Acute and Chronic Aggregate Dietary (Food and Drinking Water) Exposure and Risk Assessments for the Registration Review Risk Assessment, D448529.

S. Recore, *et.al*., 8/23/2018, MCPA: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment, D448531.

Appendix A. Toxicology Profile and Executive Summaries

A.1 Toxicology Data Requirements

The toxicology data requirements (40 CFR 158.340) for the food uses of MCPA are presented below. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

Study	Technical	
	Required	Satisfied
870.1100 Acute Oral Toxicity	yes	yes
870.1200 Acute Dermal Toxicity	yes	yes
870.1300 Acute Inhalation Toxicity	yes	yes
870.2400 Primary Eye Irritation	yes	yes
870.2500 Primary Dermal Irritation	yes	yes
870.2600 Dermal Sensitization	yes	yes
870.3100 Oral Subchronic (rodent)	yes	yes
870.3150 Oral Subchronic (nonrodent)	yes	yes
870.3200 21-Day Dermal	yes	yes
870.3250 90-Day Dermal	no	-yes
870.3465 90-Day Inhalation	yes	
870.3700a Developmental Toxicity (rodent)	yes	yes
870.3700b Developmental Toxicity (nonrodent)	yes	yes
870.3800 Reproduction	yes	yes
870.4100a Chronic Toxicity (rodent)	yes	yes
870.4100b Chronic Toxicity (nonrodent)	yes	yes
870.4200a Oncogenicity (rat)	yes	yes
870.4200b Oncogenicity (mouse)	yes	yes
870.4300 Chronic/Oncogenicity	yes	yes
870.5100 Mutagenicity—Gene Mutation – bacterial	yes	yes
870.5375 Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5550 Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a Acute Delayed Neurotoxicity (hen)	no	-
870.6100b 90-Day Neurotoxicity (hen)	no	-
870.6200a Acute Neurotoxicity Screening Battery (rat)	yes	yes
870.6200b 90-Day Neurotoxicity Screening Battery (rat)	yes	yes
870.6300 Developmental Neurotoxicity	C	yes
870.7485 General Metabolism	yes	yes
870.7600 Dermal Penetration	CR	yes
870.7800 Immunotoxicity	yes	-[A]

[A] HASPOC waiver recommendation (TXR# 0056819, J. Leshin, 11/5/2013)

A.2 Acute, Subchronic, and Chronic Toxicity Profile

The acute, subchronic, and chronic toxicity data on the MCPA, MCPA DMA, MCPA 2-EHE, and MCPA sodium salt are summarized in the tables below.

Table A2-1. Acute Toxicity Profile - MCPA Technical, EHE, Amine, Sodium salt.

Guideline No.	Study Type	MRID	Results	Toxicity Category
870.1100	Acute oral [rat] MCPA acid	00021972	LD_{50}=1.4 g/kg	III
870.1100	Acute oral [rat] MCPA 2-EHE	00156458	LD_{50}= 2.2 mg/kg	III
870.1100	Acute oral [rat] MCPA-DMA	00256980	LD_{50}=1.9 g/kg	III
870.1100	Acute oral [rat] MCPA Na salt	00256979	LD_{50}= 3.5 g/kg	III
870.1200	Acute dermal [rabbit] MCPA acid	00250090	LD_{50} > 2000 mg/kg	III
870.1200	Acute dermal [rabbit] MCPA 2-EHE	00156459	LD_{50} > 2000 mg/kg	IV
870.1200	Acute dermal [rabbit] MCPA-DMA	00256980	LD_{50} > 2000 mg/kg	IV
870.1200	Acute dermal [rabbit] MCPA Na salt	00256979	LD_{50} > 2000 mg/kg	IV
870.1300	Acute inhalation [rat] MCPA acid	40053101	LC_{50} > 6.3 mg/L[A]	IV
870.1300	Acute inhalation [rat] MCPA 2-EHE	00156460	LC_{50} > 3.1 mg/L[A]	IV
870.1300	Acute inhalation [rat] MCPA-DMA	42113103	LC_{50} > 1.7 mg/L	III
870.2400	Acute eye irritation [rabbit] MCPA acid	00250090	Corneal opacity and conjunctival irritation	I
870.2400	Acute eye irritation [rabbit] MCPA-2EHE	00115522	No evidence of eye irritation	IV
870.2400	Acute eye irritation [rabbit] MCPA-DMA	00248567	Corneal opacity	I
870.2400	Acute eye irritation [rabbit] MCPA Na salt	00256979	Corneal opacity, stippling, puckering,	II
870.2500	Acute dermal irritation [rabbit] MCPA acid	00250090	Non-irritating	IV
870.2500	Acute dermal irritation [rabbit] MCPA 2-EHE	00156456	Non-irritating	IV
870.2500	Acute dermal irritation [rabbit] MCPA DMA	00256980	Slight dermal irritation	III
870.2500	Acute dermal irritation [rabbit] MCPA Na Salt	00256979	Non-irritating	IV

Table A2-1. Acute Toxicity Profile - MCPA Technical, EHE, Amine, Sodium salt.				
Guideline No.	**Study Type**	**MRID**	**Results**	**Toxicity Category**
870.2600	Skin sensitization [Guinea Pig] MCPA acid	43062806	Not a skin sensitizer	IV
870.2600	Skin sensitization [Guinea Pig] MCPA 2-EHE	40352001	Skin sensitizer	IV
870.2600	Skin sensitization [Guinea Pig] MCPA DMA	40352101	Not a skin sensitizer	IV
870.2600	Skin sensitization [Guinea Pig] MCPA Na Salt	41613003	Not a skin sensitizer	IV

[A] 4-hour

Table A-2-2a. Subchronic and Chronic Toxicity Profile – MCPA acid[17]		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3100 90-Day oral toxicity in rats with MCPA	MRID 00165471 (1985) Acceptable/guideline 0, 50, 150, or 450 ppm (equivalent to 0, 3.6, 10.9, or 32.6 mg/kg/day for males and 0, 4.0, 12.1, or 35.8 mg/kg/day for females).	NOAEL = 10.9 mg/kg/day LOAEL = 32.6 mg/kg/day based on increased absolute and relative kidney weights, increased clotting time, increased creatinine levels, and presence of crystaluria (oxalate, calcium phosphate, and urate).
870.3150 90-Day oral toxicity in dogs with MCPA	MRID 00106595 (1980) Acceptable/guideline main study technical MCPA 0, 77-86, 300-342, or 1198- 1370 ppm (equivalent to 0, 3.0, 12.0, or 48.0 mg/kg/d). second study technical MCPA 0, 7.5, 25.0, and 300.0 ppm (equivalent to 0, 0.3, 1.0, or 12.0 mg/kg/d)purified MCPA–	NOAEL = 1 mg/kg/day LOAEL = 3 mg/kg/day, based on impaired renal function, without histopathological change.

[17] NOAEL/LOAEL values may not reflect the current practices. NOAEL/LOAEL values were updated during registration review only for studies identified for endpoint selection.

Table A-2-2a. Subchronic and Chronic Toxicity Profile – MCPA acid[17]		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3200 21-day dermal-rabbit with MCPA	42715001 (1992) acceptable/guideline 10, 100, or 1000 mg/kg/day	Systemic toxicity NOAEL = 100 mg/kg/day LOAEL = 1000 mg/kg/day (limit dose) based on kidney findings (increase in incidence of mineralization in renal tubule) and the decrease in body weight gain Dermal toxicity NOAEL = 10 mg/kg/day LOAEL = 100 mg/kg/day based erythema, desquamation, and diffuse acanthosis
870.3465 28-day inhalation toxicity in rats with MCPA	48606401 (2011) Acceptable/non-guideline* 0, 0.05, 0.2 and 1.0 mg/L for 6 hours per day; reduced to 0, 0.02, 0.1 and 0.5 mg/L following 3 (females) or 4 (males) exposures due to severe toxicity *non-guideline status is because the MMAD for the test atmospheres especially for the mid and high dose exposures did not have a sufficient percentage of particles less than the recommended 3 microns. Since the study did not demonstrate a NOAEL for alterations in the upper respiratory tract and because of the several responses to treatment, the issue of unacceptable particle size has added importance.	Portal of entry toxicity LOAEC = 0.02 mg/L/day (both sexes), based on epithelial alteration in the larynx. NOAEC not established for portal of entry effects Systemic toxicity Systemic LOAEL = 0.1 mg/L. At the mid and high dose levels there was squamous cell metaplasia of the larynx and in the nasal cavity, diffuse tubular degeneration of the testes, increase of oligospermia and debris in the epididymides, and follicular hypertrophy/ hyperplasia of the thyroid gland and increased absolute/relative thyroid weight, deceased absolute and relative thymus weight in females, and decreased absolute (both sexes) and relative (females) spleen weight, alterations in RBC and WBC elements, increased prothrombin time and altered clinical chemistry parameters (glucose and urea). There were reductions in rearing in both sexes and lower motor activity (in females). Systemic NOAEC level was 0.02 mg/L.

Table A-2-2a. Subchronic and Chronic Toxicity Profile – MCPA acid		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3700a Prenatal developmental in rats with MCPA	42723801 (1993) acceptable/guideline 15, 60, and 120 mg/kg/day.	maternal toxicity NOAEL = 120 mg/kg/day LOAEL = not identified. developmental toxicity NOAEL = 60 mg/kg/day. LOAEL = 120 mg/kg/day based on decreased fetal body weights and an increase in the number of fetuses with skeletal retardation.
870.3700b Prenatal developmental in rabbits with MCPA	42723802 (1993) acceptable/guideline 15, 30, and 60 mg/kg/day.	maternal toxicity NOAEL ≥ 60 mg/kg/day. LOAEL = not identified. developmental toxicity NOAEL > 60 mg/kg/day (HDT) LOAEL = not a developmental toxicant
870.3800 Reproduction and fertility effects in rats with MCPA	40041701 (1986) acceptable/guideline 0, 50, 150, or 450 ppm (equivalent to 0, 2.5, 7.5, and 22.5 mg/kg/day, respectively, for both sexes based on 1 ppm = 0.05 mg/kg/day).	Parental systemic toxicity NOAEL =22.5 mg/kg/day (HDT) LOAEL = not identified Offspring toxicity NOAEL =7.5 mg/kg/day LOAEL =22.5 mg/kg/day based on decreased pup weight during lactation Reproductive toxicity NOAEL =22.5 mg/kg/day (HDT) LOAEL = no LOAEL was established.
870.4.300 Chronic toxicity and carcinogenicity in rats with MCPA	40634101 (1988) acceptable/guideline 0, 20, 80, or 320 ppm for 2 years (0, 1.1, 4.4, or 17.6 mg/kg/day in males and 1.4, 5.7, or 23 mg/kg/day in females)	NOAEL = 4.4 mg/kg/day LOAEL= 17.6 mg/kg/day based on nephrotoxicity (increased urea nitrogen in females) were observed. In addition, there was an increase in the retraction and granular surface of the kidney associated with an increase in the chronic progressive nephropathy in the males. At the doses tested, there was not a treatment related increase in tumor incidence when compared to controls. Dosing was considered adequate.

70.4100b Chronic toxicity dogs with MCPA	00164352 (1986) acceptable/guideline 0, 6, 30, 150 ppm (0, 0.2, 1.02, or 5.32 mg/kg/day for males and 0, 0.21, 1.02 or 5.12 mg/kg/day for females)	NOAEL = 0.2 mg/kg/day LOAEL= 1.02 mg/kg/day based on hepatotoxicity (increased SGPT, SGOT, triglycerides and cholesterol levels with histopathology changes) and nephrotoxicity (increased urea nitrogen, potassium, and creatinine levels with histopathology changes (increased pigmentation of the proximal tubular epithelium) in kidneys].
870.4300 Chronic toxicity and carcinogenicity in mice with MCPA	40792301 (1988) acceptable/guideline 0, 20, 100, or 500 ppm (0, 3.2, 15.7, or 79.5 in males and 0, 3.9, 19.5, or 97.2 mg/kg/day) for 2 years.	Males: NOAEL = 15.7 mg/kg/day LOAEL= 79.5 mg/kg/day based on histopathology changes in kidneys Females: NOAEL = 3.9 mg/kg/day LOAEL= 19.5 mg/kg/day based on renal hyperplasia At the doses tested, there was not a treatment related increase in tumor incidence when compared to controls. Dosing was considered adequate.
870.6200a Acute oral neurotoxicity in rats with MCPA	43562602 (1994) Acceptable/guideline 0, 200, 400, or 800 mg/kg (males) 0, 150, 300, or 600 mg/kg (females) via gavage.	LOAEL = 400 mg/kg, based on gait impairment, decreased activity and abdominal tension in male rats NOAEL = 200 mg/kg.
870.6200b Subchronic oral neurotoxicity in rats with MCPA	43562601 (1994) acceptable/guideline 0, 50, 500, and 2500 ppm (equivalent to 0, 3, 34, or 177 mg/kg/day for males and 0, 4, 42, or 188 mg/kg/day for females).	NOAEL = 34 mg/kg/day LOAEL= 177 mg/kg/day based on based on decreased body weight and body weight gains, liver pathology, changes in clinical chemistry and hematological parameters, testicular atrophy, reduced values of forelimb grip strength (day 50 only) and reduced values in the foot splay test (day 22 only) in males and reduced values of hindlimb grip strength in females.
Gene mutation 870.5265	42840403 (1993) acceptable/guideline *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 Tested up to 5,000 μg/plate	The test was negative.
870.5300 Gene mutation– Chinese hamster ovary cells (CHO/HGPRT)	42860103 (1993) Acceptable/guideline *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 Tested up to 5,000 μg/plate	The test was negative.

870.5915 *In Vivo* Mammalian Cytogenetics - Sister Chromatid Exchange assay	00148720 (1985) Acceptable/guideline Dose: 1200 mg/kg	The test was weakly positive.
870.5385 *In Vivo* Mammalian Cytogenetics - Chromosomal aberration	40027501 (1986) Acceptable/guideline 0, 33, 200 or 1200 mg/kg body weight.	The test was negative.

Table A-2-2a. Subchronic and Chronic Toxicity Profile – MCPA acid

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.5375 cytogenetic assay (human lymphocytes)	42853504 (1993) Acceptable/guideline S9-activated doses of 1200-2000 ug/mL (13 hr cell harvest) that approached the solubility limit.	The test was positive. The non-activated test material was cytotoxic (>500 ug/mL-21 hr cell harvest), but not clastogenic.
870.7600 Dermal absorption in rats	46327601 (2003) Acceptable/guideline 0.09 mg/cm^2 and 7.5 mg/cm^2	Over all recovery was good ranging from 90.35% to 95.46% for the low dose and 94.43% to 96.85 % for the high dose. For the low dose the majority of absorbed dose was excreted in the urine with the second highest portion in the carcass. For the high dose the absorbed test compound accumulated in the carcass with the highest portion at 10 hours (22.08%). At 96 hours 12.86% remained in the carcass and 12.28% was excreted in the urine. This pattern indicates saturation of excretion at the high dose.
870.7600 Dermal penetration *in vitro* human and rat	45897010 (2002) Acceptable/guideline Radioactive MCPA was combined with a MCPA DMA formulation (concentrated or as a diluted aqueous spray) and applied to human and rat epidermal membranes. Actual doses of 7520 µg/cm2 and 94.3 µg/cm2 were utilized for the concentrated and diluted groups, respectively. The exposure duration for the human and rat skin samples were 8 hours and 24 hours.	Results indicated that a greater proportion of the applied MCPA dose was absorbed through both human and rat epidermis with the diluted formulation (10.4% and 30.6% of the applied dose at 24 hours for human and rat skin, respectively) compared to the concentrated formulation (2.96% and 11.5% of the applied dose at 24 hours for human and rat skin, respectively).

Table A-2-2b. Subchronic and Chronic Toxicity Profile – MCPA DMA[16]		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3150 90-Day oral toxicity in dogs with MCPA-DMA	43556802 (1995) Acceptable/guideline 20, 80, and 360 ppm (equivalent in the males to 0, 0.6, 2.4 and 10.9 mg/kg/day and in the females to 0, 0.7, 2.9, and 12.8 mg/kg/day)	NOAEL = 0.6 MCPA DMA (0.4 as MCPA acid) mg/kg/day. LOAEL = 2.4 MCPA DMA (2.0 as MCPA acid) mg/kg/day, based on changes in histopathology (increases in subacute to chronic interstitial inflammation of liver), hematology, and clinical chemistry (BUN, creatinine, ALT, partial thromboplastin times)
870.3200 21-day dermal-rat with MCPA DMA	43556902 (1995) acceptable/guideline 12, 120, or 1000 mg/kg/day	Systemic toxicity NOAEL =not observed at 1000 mg/kg/day (limit dose) LOAEL = not observed at 1000 mg/kg/day (limit dose) Dermal toxicity NOAEL = 120 mg/kg/day LOAEL = 1000 mg/kg/day
870.3700a Prenatal developmental in rats with MCPA DMA	44954102 (1999) acceptable/guideline 0, 15, 50, or 150 mg MCPA free acid kg/day (0, 18.5, 62 and 185 mg/kg/day MCPA DMA)	maternal toxicity NOAEL = 50 mg/kg/day LOAEL = 150 mg/kg/day based on mortality and clinical signs (rocking, lurching, or swaying, hunched appearance, dried yellow matting/staining on the urogenital area), post-implantation loss and increased resorptions (primarily early). developmental toxicity NOAEL = 50 mg/kg/day. LOAEL = 150 mg/kg/day based on increased resorptions (primarily early), post-implantation loss, decreased fetal body weight, and external and skeletal malformations/variations
870.6200a Acute oral neurotoxicity in rats with MCPA DMA salt	43562702 (1994) Acceptable/guideline 0, 175, 350, or 700 MCPA DMA salt mg/kg (equivalent to 0, 142, 285, or 569 MCPA free acid mg/kg)	LOAEL = 175 mg/kg (equivalent to 142 MCPA Acid mg/kg) (LDT) seen in female rats based on ataxia. NOAEL could not be established.
870.6200b Subchronic oral neurotoxicity in rats with MCPA DMA	43562701 (1994) acceptable/guideline 0, 60, 600, or 3,000 ppm (equivalent to 0/0, 4/5, 42/48, or 208/232 MCPA DMA mg/kg/day [M/F]; 0/0, 3.2/4.1, 34/39, or 169/189 MCPA acid mg/kg/day).	NOAEL = 34 mg/kg/day LOAEL= 169 mg/kg/day based on decreased body weight and body weight gains, liver pathology, testicular atrophy, and changes in clinical chemistry (ALT, AST, ALP, creatinine), hematological parameters and neurotoxicity (decreased forelimb grip strength).

Table A-2-2b. Subchronic and Chronic Toxicity Profile – MCPA DMA[16]		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3465 28-day inhalation toxicity in rats with MCPA DMA	48952902 (2012) Acceptable/guideline Nose-only: aerosol administered to male and female WIST(SPF) rats for 6 hours/day, 5 days/week for 4 weeks at actual exposure concentrations of 0, 0.01, 0.02, or 0.05 mg/L (as MCPA)	NOAEC = not identified LOAEC = 0.01 mg/L based on respiratory tract effects (bronchial/bronchiolar hyperplasia/hypertrophy, interstitial cell infiltration and peribronchiolar fibrogenesis) and increased lung weights.
870.3465 28-day inhalation toxicity in rats with MCPA DMA	48952903 (2012) Acceptable/guideline Nose-only. Aerosol administered hours/day, 5 days/week for 4 weeks at actual exposure concentrations of 0, 0.051, 0.149, or 0.514 mg/L (as MCPA)	Portal of Entry NOAEC = not identified. LOAEC = 0.051 mg/L based on respiratory tract effects (bronchial/bronchiolar hyperplasia/hypertrophy, interstitial cell infiltration and peribronchiolar fibrogenesis) and increased lung weights. Note: Adrenal and thymus effects were considered stress related.
870.5265 Gene Mutation - bacterial	42624401 (1992) Acceptable/guideline *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 Concentrations at 1, 4, 16, 64, or 256 µg/plate in the presence or absence of S9-activation.	The test was negative.
870.5300 Gene mutation– Chinese hamster ovary cells (CHO/HGPRT)	42860101 (1993) Acceptable/guideline Up to 2500ug/mL with or without S9 activation	The test was negative.
870.5375 cytogenetic assay (human lymphocytes)	42853505 (1993) Acceptable/guideline Dose range: S9-activated doses of 250, 1000, or 2000 ug/mL (13 hr cell harvest) that approached the solubility limit.	The test was positive. The non-activated test material was not clastogenic.
870.5395 Micronucleus assay	42853502 (1993) Acceptable/guideline 144, 288, or 576 mg/kg/day.	The test was negative.

Table A-2-2b. Subchronic and Chronic Toxicity Profile – MCPA DMA[16]		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.7600 Dermal absorption in rats	44193901 (1996) Acceptable/guideline DMA: 0.02, 0.19, 0.97, 4.66 mg acid equivalents/cm^2	DMA: dermal penetration was 0.35%, 1.05%, 2.79%, and 5.04% (with increasing dose) of the administered dose following 10-hr exposures and 1.01%, 3.42%, 6.02%, and 13.24%, respectively following a 24-hour exposure. At the 10 hr exposure, the amount of radioactivity remaining on the application site of the skin (skin-bound residues) was 30.27, 18.20, 2.30 and 2.85% of the administered dose. At the 24 hr exposure, the amount of radioactivity remained on the application site of the skin (skin-bound residues) was 29.17, 16.47, 4.91 and 4.84% of the administered dose.

Table A-2-2c. Subchronic and Chronic Toxicity Profile – MCPA 2-EHE[16]		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3150 90-Day oral toxicity in dogs with MCPA 2-EHE	43556801 (1995) Acceptable/guideline 0, 20, 80, and 360 ppm (equivalent in the males	NOAEL = 0.6 MCPA 2-EHE (0.4 as MCPA acid) mg/kg/day. LOAEL = 2.5 MCPA 2-EHE (1.6as MCPA acid) mg/kg/day based on changes in clinical
870.3700a Prenatal developmental in rats with MCPA 2-EHE	44954101 (1999) acceptable/guideline 0, 15, 40, and 120 mg MCPA free acid kg/day (0, 23.5, 62.7, and 188.0 mg MCPA 2-EHE/kg/day)	<u>maternal toxicity</u> NOAEL = 40 mg/kg/day (MCPA acid equiv) LOAEL = 120 mg/kg/day based on total litter resorptions (primarily early) and postimplantation loss. <u>developmental toxicity</u> NOAEL = 40 mg/kg/day. LOAEL = 120 mg/kg/day based on total litter resorptions (primarily early), postimplantation loss, decreased fetal weight, and skeletal malformations/variations.
870.6200a Acute oral neurotoxicity in rats with MCPA 2-EHE	43556702 (1994) Acceptable/guideline* 0, 250, 500, or 1000 mg/kg all clinical sings were reversible by day 14 post exposure; therefore, although the study failed to identify a NOAEL, the study is considered acceptable and the LOAEL for clinical findings is useful for acute reference dose consideration for future risk assessment.	LOAEL = 250 mg/kg (LDT) for male and female rats, based on FOB effects (alterations in gait and activity). NOAEL was not identified. At higher doses (500 mg/kg for male rats and 1000 mg/kg for female rats) decrease in body weight gain was observed.

Table A-2-2c. Subchronic and Chronic Toxicity Profile – MCPA 2-EHE[16]		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.6200b Subchronic oral neurotoxicity in rats with MCPA 2-EHE	43556701 (1994) acceptable/guideline 0, 75, 750, or 3750 ppm (equivalent to 0/0, 5/6, 54/63, or 261/296 MCPA 2-EHE mg/kg/day [M/F]; 0/0, 3.2/3.8, 34.6/40.4, or 167/190 MCPA Acid mg/kg/day).	NOAEL = 34.6 mg/kg/day LOAEL= 167 mg/kg/day based on focal testicular atrophy, increased relative kidney weight, decreased body weight, clinical chemistry changes, and decreased motor activity in males.
870.5265 Gene mutation MCPA 2- EHE	42870001 (1993) Acceptable/guideline *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA1538 Tested up to 5,000 µg/plate	The test was negative.
870.5300 Gene mutation– Chinese hamster ovary cells (CHO/HGPRT) MCPA 2-EHE	42860102 (1993) Acceptable/guideline Up to limit of solubility in culture medium (200 ug/mL) with or without S9 activation	The test was negative.
870.5375 cytogenetic assay (human lymphocytes) MCPA 2-EHE	42853506 (1993) Acceptable/guideline 20-160ug/mL -S9; 40-132ug/mL +S9	The test was negative.
870.6300 Developmental neurotoxicity in rats	48606401 (2010) Acceptable/guideline 0, 300, 900, or 1800 ppm during gestation	No evidence of developmental neurotoxicity <u>Maternal toxicity</u> LOAEL = 1800 ppm (156 mg/kg/day),
MCPA 2-EHE	0, 200, 600, or 1200 ppm during lactation (equivalent to 28, 83, and 156 mg/kg/day, gestation/lactation) from gestation day (GD) 6 through lactation day (LD) 21.	based on decreases in body weight, body weight gain, and food consumption. Maternal NOAEL = 900 ppm (83 mg/kg/day). <u>Offspring toxicity</u> Offspring LOAEL = 1800 ppm (156 mg/kg/day), based on decreases in body weight and body weight gain and an increase in pup mortality. Offspring NOAEL = 900 ppm (83 mg/kg/day).
870.7600 Dermal absorption in rats MCPA 2-EHE	44193901 (1996) Acceptable/guideline EHE: 0.19 mg acid equivalents/cm^2	EHE: dermal penetration was 10.69% of administered dose following a 24-hour exposure

Appendix B. Physical/Chemical Properties

Table B. Physicochemical Properties of MCPA.				
Parameter	Value			Reference
	MCPA	**MCPA DMAS**	**MCPA 2-EHE**	
Melting point/range (Boiling point/range)	114-119 °C	(111 °C)	(260-265 °C)	MCPA RED, PC Chapter (D299360, F. Fort, 6/3/2004)
pH	approximately 3 [MCPA Reregistration Standard, PC Chapter]	Not available	3.46 at 19.7 °C [D202560, 6/20/2003)]	[See specific column]
Density, at 20 °C	1.18-1.21 g/mL	1.181 g/mL	8.9 lb/gal bulk density (1.06 g/mL specific gravity)	MCPA RED, PC Chapter
Water solubility, at 20 °C	0.03 g/100 g	Rapidly dissociates to the free phenoxy anion and dimethyl ammonium moiety in water.	<1 mg/L	MCPA RED, PC Chapter
Solvent solubility, at 20 °C	91.8 g/100 g acetone 50.2 g/100 g ethyl ether 5.5 g/100 g chloroform 3.3 g/100 g benzene	Not available	Miscible in most organic solvents and mineral oils.	MCPA RED, PC Chapter
Vapor pressure, at 20 °C	7.7×10^{-6} mbar	Not available	1.77×10^{-5} mbar	MCPA RED, PC Chapter
Dissociation constant, pK_a	3.07	3.07	NA	CB# 923, 9/12/86, W. Anthony [Task Force Data; Accession No. 962678]
Octanol/water partition coefficient, Log(K_{OW})	2.73	1.415	5.37	MCPA RED, PC Chapter
UV/visible absorption spectrum	Not available	Not available	Absorbance peaks observed at 203, 228, and 279 nm for a solution of MCPA 2-EHE in water with methanol co-solvent; molar absorption coefficient of 16784 M^{-1} cm^{-1} at λ_{MAX} 203.1 nm.	D202560

Appendix C. Maximum Residue Limits

MCPA: Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition:				
US		Canada	Mexico[2]	Codex
40 CFR 180.339: *Compliance with the tolerance levels specified below is to be determined by measuring only MCPA, 2-(4-chloro-2-methylphenoxy)acetic acid, in or on the commodity*		*MCPA: 2-(4-chloro-2-methylphenoxy)acetic acid*		*MCPA*
Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US	Canada	Mexico[2]	Codex[3]
Alfalfa, forage	0.50			
Alfalfa, hay	2.0			
Barley, grain	0.20	0.03		0.2
Barley, hay	50			50
Barley, straw	50			50
Clover, forage	0.50			
Clover, hay	2.0			
Corn, grain		0.01		0.01*
Corn, sweet		0.015		
Poultry, byproducts		0.05		0.05*
Poultry, fat		0.05		0.05*
Poultry, meat		0.05		0.05*
Eggs		0.05		0.05*
Flax, seed	0.01	0.01		0.01*
Grain, aspirated fractions	3.0			
Grass, forage	500			500
Grass, hay	200			
Hog, byproducts		0.05		3
Hog, fat		0.05		0.2
Hog, meat		0.05		0.1
Lespedeza, forage	0.50			
Lespedeza, hay	2.0			
Milk	0.04	0.01		0.04
Oat, forage	50			50
Oat, grain	0.20	0.03		0.2
Oat, hay	50			50
Oat, straw	50			50
Pea, dry	0.01	0.1		0.01*
Pea, field, hay	1.5			
Pea, succulent	0.10	0.1		
Pea, field, vines	0.60			
Ruminant, meat by products	3.0	0.05		3
Ruminant, fat	0.20	0.05		0.2
Ruminant, meat	0.10	0.05		0.1
Rye, forage	50			50
Rye, grain	0.20	0.03		0.2
Rye, straw	50			50
Trefoil, forage	0.50			
Trefoil, hay	2.0			
Triticale, grain	0.50			0.2

MCPA: Summary of US and International Tolerances and Maximum Residue Limits				
Residue Definition:				
US		Canada	Mexico[2]	Codex
Triticale, straw†	2.0			50
Vetch, forage	0.50			
Vetch, hay	2.0			
Wheat, forage	50			50
Wheat, grain	0.20	0.03		0.2
Wheat, hay	50			50
Wheat, straw	50			50
Completed: D. Nadrchal 7/24/2018				

[1] Tolerance values are the HED recommendations and not necessarily the currently established levels.
[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.
[3] *Codex additional description of "*At or about the limit of determination*"
† Wheat commodity definition in CFR 180.1 (g) includes triticale

Appendix D. Review of Human Research

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include [studies from PHED 1.1; the AHETF database; the Outdoor Residential Exposure Task Force (ORETF) database; the ARTF database; the Residential SOPs (Lawn/Turf); other registrant-submitted exposure monitoring studies (446557-02, 450331-01)], are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[18].

[18] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure

Appendix E. Search Parameters for MCPA Toxicology Literature Review

Date and Time of Search: 11/01/2017; 9:15 am
Search Details:
((MCPA)) AND (rat OR mouse OR dog OR rabbit OR monkey OR mammal)
PubMed hits: 248
Number of Swift Articles: 142 for Animal
Number of Swift Articles: 162 for Human
Number of Swift Articles: 0 for No Tag